The Effects of Family Support, Anxiety, and Post-Treatment Nausea on the Development of Anticipatory Nausea: A Latent Growth Model

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Abstract
Although the degree of a patient’s anxiety and symptoms of post-treatment nausea have been suggested as predictors of anticipatory nausea, little attention has been given to the impact of family support on the development of anticipatory nausea. This study examines the role of family support in the development of the severity of anticipatory nausea, both directly and mediated through a patient’s anxiety. Five hundred thirty-nine patients with breast cancer were studied. The results from latent growth modeling showed that family support was associated with the severity of anticipatory nausea mediated by the levels of a patient’s anxiety and post-treatment nausea severity. In addition, family support had a direct impact on the severity level of anticipatory nausea. The findings suggest that helping patients and their families communicate in more satisfactory and supportive ways and maintain an organized family system might be beneficial in reducing the symptoms of chemotherapy-related nausea.

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Key Words
Family support, anxiety, development of chemotherapy-related nausea, anticipatory nausea

Introduction
Nausea, a subjective, unpleasant feeling that may trigger vomiting, is one of the most frequently reported and troublesome adverse effects of chemotherapy for cancer.1,2 Chemotherapy-related nausea detracts significantly from a patient’s quality of life and may even lead to a discontinuation or avoidance of treatments.3 Post-treatment nausea is assumed to have pharmacological as well as psychological causes, whereas anticipatory nausea is assumed to be a conditioned response that is psychological in origin.4–7 Despite the use of increasingly potent antiemetic medications, such as 5-HT3 receptor antagonists, the prevalence of nausea remains high.8 Exploring psychological contributions to chemotherapy-related nausea, particularly to anticipatory nausea, may give hope
that nonpharmacological or psychological methods to relieve the symptoms are efficacious.

Experiencing symptoms of post-treatment nausea has been assumed to be a necessary factor in the association (conditioning) process of development of anticipatory nausea. In addition, researchers have given much attention to anxiety as a significant psychological predictor of anticipatory nausea. It has been found that anxiety predisposes some individuals to learn quickly the association between certain stimuli and the drug-induced side effects of post-treatment nausea, thereby contributing to the conditioned response of anticipatory nausea. However, psychosocial predictors of the development of a patient’s anxiety and the associated chemotherapy-related nausea across treatments have been given relatively little attention.

A plethora of studies has shown that social support plays a beneficial role in a patient’s psychological and physical adjustment to various diseases, including cancer (for review, see Refs. 10,11). Among the several forms of social support, family support has been found to be the most important resource in a patient’s adjustment to cancer.12,13 Family support is generally viewed as the degree to which family members relate to and communicate with each other, pursue goals, organize activities, and perform family routines and procedures.14

A number of studies have found that a patient’s psychological adjustment to cancer is better in a family characterized by cohesiveness, open expression, and absence of conflict.12,15–18 These family characteristics have been associated with a patient’s lower level of anxiety (see Refs. 15,16) and reduced chemotherapy-related symptoms, including fatigue and nausea.15,17,19 In addition to these family relationship characteristics, the family system, such as role flexibility and how the family is structured,14 also has influenced the patient’s ability to adapt to the demands of cancer and its treatment.19

The results from these studies suggest that the characteristics of family relationships and the family system are associated with the patient’s psychological and physical adjustment, such as anxiety and chemotherapy-related nausea. However, none of these studies has examined the associations among these factors in a simultaneous and longitudinal model.

Thus, to date, no study has examined how family relationships facilitate or inhibit the development of a patient’s symptoms of anticipatory nausea in a more complete model that includes the development of the patient’s anxiety and symptoms of post-treatment nausea.

The prospective design in the current study allows us to examine predictors of development of anticipatory nausea. The model tested (Fig. 1) includes six specific hypotheses: (a) post-treatment nausea from previous treatment will be associated with the development of anticipatory nausea symptoms after treatment; (b) a patient’s anxiety will be related to the development of anticipatory nausea symptoms; (c) a patient’s anxiety will trigger the conditioning process of development of anticipatory nausea symptoms via the development of post-treatment nausea symptoms; (d) a supportive family environment will be inversely associated with a patient’s anxiety, which in turn, reduces the development of a patient’s anticipatory nausea symptoms; (e) a supportive family environment will be inversely related to a patient’s anxiety, which in turn, reduces the development of a patient’s post-treatment nausea symptoms, which further reduces the development of a patient’s anticipatory nausea symptoms; (f) finally, a supportive family environment may be directly associated with less development of a patient’s anticipatory nausea symptoms, above and beyond the impact of his/her anxiety and development of post-treatment nausea symptoms. The last hypothesis is explorative due to lack of supportive findings in the existing literature.

The conceptual model provided in Fig. 1 will be tested using a latent growth structural model,20,21 including lagged effects among measures. This model allows us to examine
cross-lagged effects among anxiety, post-treatment nausea, and anticipatory nausea. More importantly, this model allows us to distinguish the effects of individual differences in the patient’s anxiety and symptoms of chemotherapy-related nausea at the initial treatment of chemotherapy from the effects of changes in anxiety and nausea symptoms over treatments. For example, the hypothesis (f) can be examined if supportive family environment is associated with the initial level of a patient’s symptoms of anticipatory nausea or with the change (slope) of a patient’s symptoms of anticipatory nausea across treatments. The latent growth structural modeling procedure will help clarify predictors of the development of anticipatory nausea.

**Methods**

**Participants**

Patients who had received treatment with either cyclophosphamide and oxorubicin with or without 5-fluorouracil (CA/CAF), or cyclophosphamide, methotrexate, and 5-fluorouracil (CMF), for five consecutive chemotherapy cycles, were included in the current study to control for differential side effects of receiving different chemotherapy regimens (see Ref. 22 for detailed recruitment information). Four male breast cancer patients and eight patients who had missed any assessment during the first five treatments were excluded (see Appendix, no. 1). Thus, the present study sample consists of the 539 female patients with breast cancer who had received and completed five chemotherapy treatments from Hickok et al.’s sample.

Each treatment was three to four weeks apart following the standard protocol for administering the chemotherapy regimen, thus an average timing of the five treatments was 18 weeks. The average age of the 539 patients was 51 years (range 24–83), and most patients were married (75%), Caucasian (94%), and had at least a high school education (93%).

**Measures**

**Family Support.** The Family Environment Scale (FES) assesses the environment in which a family creates and imposes expectations and demands for behavior upon its members, and was used to assess the degree to which a patient perceives support from the family. Five subscales that assess family relationships and the family system (45 items), which have been found in existing studies to be associated with a patient’s adjustment, were selected as measures of supportiveness of the family environment. Three of these subscales (cohesion, expressiveness, and conflict) describe characteristics of family relationships. According to Moos and Moos, cohesion is the degree of commitment, help, and support that family members provide for one another. Expressiveness is the extent to which family members are encouraged to act openly and to express their feelings directly. Conflict is the amount of openly expressed anger, aggression, and disagreement among family members. The other two subscales (organization and control) are part of a construct domain generally seen as system maintenance. Organization is outlined as the degree of importance of clear organization and structure in planning family activities and responsibilities. Control is the extent to which set rules and procedures are used to regulate family life. The psychometric properties and validity of the FES have been established.

**Anxiety.** The extent to which the patients experienced nervousness, tension, and other correlates of anxiety was measured using the State and Trait Anxiety Inventory (STAI) which is a self-report inventory with 20 items each for trait and state anxiety. Items are rated on a 5-point scale of distress (0–4), ranging from “not at all” to “extremely.” Only the state anxiety score was included in the analyses. The STAI has been widely used, and its reliability and validity have been well documented. The test-retest reliability of the STAI across four assessments in the present study ranged from 0.56 to 0.64.

**Severity of Post-Treatment and Anticipatory Nausea.** The Morrow Assessment of Nausea and Emesis (MANE) was used to assess nausea. The MANE is a patient self-report measure of severity (measured on a 6-point scale from 0 = “not at all” to 6 = “intolerable”) of both post-treatment and anticipatory nausea. The scale has been used in over two dozen recent research
studies, and its psychometric validity and reliability have been established.\textsuperscript{26,27} The test-re-test reliability of the MANE ranged from 0.46 to 0.58 for post-treatment nausea, and 0.29 to 0.34 for anticipatory nausea.

**Emetic Potential Score ofChemotherapy Drugs.** A clinical rating of the emetic potential of the patient’s chemotherapy drug was calculated. Devised at the University of Rochester Medical Center by the Cancer Center pharmacist and nurse-clinicians, an emetic score from 0 (no emetic potential) to 4 (maximum emetic potential) was assigned to 53 drugs commonly used for chemotherapy. A sum of emetic scores of chemotherapy regimen for each patient was calculated to serve as a covariate in the present study.

**Procedure**

The study was approved by the University of Rochester Institutional Review Board (IRB), as well as the IRBs of all participating institutions. Eligible patients were recruited from different community hospitals at the time of their first chemotherapy treatment. Patients who agreed to join the study signed a consent form, and demographic and clinical data were gathered from medical charts. At the second chemotherapy treatment (before drugs were administered to the patient), the patient completed the FES and the anxiety measure. The patient also completed the MANE regarding the first treatment. A questionnaire packet, including the anxiety measure and the MANE, was then given to the patient to complete after each chemotherapy treatment up to and including the fifth treatment. Patients were asked to return these questionnaires one week after each chemotherapy treatment using a stamped, self-addressed envelope. Compliance with this procedure was high; on the rare occasion that a participant failed to return the form(s), a reminder contact was made by phone.

**Results**

**Model Specification**

Means and standard deviations of study variables are reported in Table 1. Internal consistencies of measures included in the present study to measure the proposed four latent variables (see Fig. 1) were examined using structural equation modeling (AMOS 5.0).\textsuperscript{28} Units of the study variables were quite different from each other, so the study variables were standardized separately before included in the model. Therefore, centering study variables was not required. The family support latent variable was measured by the five subscales of the FES. The repeated measures of anxiety, post-treatment nausea, and anticipatory nausea were each modeled as a two-parameter latent growth structural model (i.e., initial level [intercept] and average rate of change [slope] across the five treatments: see the next paragraph for the description of the model specification). Each latent variable was specified with their initial levels and their changes from the first to the fifth treatments for anxiety and post-treatment nausea; and from the second to the fifth treatments for anticipatory nausea. In addition, a covariate of emetic potential rating score of the chemotherapy

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Means (SDs) of Study Variables (n = 539)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Tx1</td>
</tr>
<tr>
<td>Family Environment Scale</td>
<td></td>
</tr>
<tr>
<td>Cohesion</td>
<td>57.75 (12.83)</td>
</tr>
<tr>
<td>Expression</td>
<td>54.74 (12.16)</td>
</tr>
<tr>
<td>Conflict</td>
<td>42.29 (10.39)</td>
</tr>
<tr>
<td>Organization</td>
<td>54.84 (11.88)</td>
</tr>
<tr>
<td>Control</td>
<td>46.87 (10.75)</td>
</tr>
<tr>
<td>Emetic score</td>
<td>5.35 (0.94)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>38.24 (11.97)</td>
</tr>
<tr>
<td>Severity of nausea</td>
<td></td>
</tr>
<tr>
<td>Post-treatment</td>
<td>1.78 (1.59)</td>
</tr>
<tr>
<td>Anticipatory</td>
<td>0.33 (0.87)</td>
</tr>
</tbody>
</table>

*Tx = Chemotherapy treatment.*
regimen was included in the model to predict both levels and slopes of chemotherapy-related nausea.

To decipher the characteristics of the development of nausea using latent growth structural modeling, two latent components each of anxiety, post-treatment nausea, or anticipatory nausea were specified, as shown in Fig. 2. The overall model includes separate growth trajectories across treatments for anxiety, post-treatment nausea, and anticipatory nausea. Each trajectory is modeled as a linear function of chemotherapy treatments, with the intercepts estimating participants’ predicted levels of anxiety and post-treatment nausea at treatment one and of anticipatory nausea at treatment two. The slope latent variables reflect participants’ average rates of change across treatment in these three measures. For each measure, the loading of the assessments was fixed to 1 for the “intercept” latent variable; fixed to 0, 1, 2, 3, and 4 for the anxiety and post-treatment nausea “slope” latent variables; and fixed to 0, 1, 2, and 3 for the anticipatory nausea “slope” latent variable. “Intercept” and “slope” latent variables for each of anxiety, post-treatment nausea, or anticipatory nausea were allowed to covary. The error variances of observed variables were estimated. In addition, variables assessed at the same treatment were allowed to have correlated errors (time-specific error terms). All other off-diagonal elements in the measurement error matrices were fixed to zero.

Furthermore, to examine the impact of an observed variable at a certain treatment on another observed variable at the subsequent treatment, cross-lagged effects among anxiety, post-treatment nausea, and anticipatory nausea were included. We regressed the measure of one variable at a target treatment onto the other variable at the previous treatment (e.g., regressed the severity of anticipatory nausea at treatment two onto the anxiety at treatment one or the severity of post-treatment nausea at treatment one).

**Test of Measurement Fit**

A confirmatory one-factor factor analysis using a structural equation model established that all five subscales of the FES loaded significantly on one family support construct. At this point, we noted that the assumption of multivariate normality was violated, multivariate kurtosis = 6.05, \( P < 0.001 \). Thus, we implemented Bollen-Stine (BS) bootstrap for correcting Chi-square. The following five model fit indices were used in the present study: the

![Fig. 2](image_url)  
**Fig. 2.** Regression weights from latent growth structural analysis of predicting severity of anticipatory nausea. ANX_I = Intercept of Anxiety; ANX_S = Slope of Anxiety; PNS_I = Intercept of Post-treatment Nausea Severity; PNS_S = Slope of Post-treatment Nausea Severity; ANS_I = Intercept of Anticipatory Nausea Severity; ANS_S = Slope of Anticipatory Nausea Severity; EPR = Emetic potential rating score of chemotherapy regimen; Solid highlighted paths and the corresponding path coefficients are significant at \( P < 0.05 \); Measurements, measurement errors, covariances, and cross-lagged effects were included in the analysis (see the text for details), but are omitted from the figure for graphic simplicity.
standardized root mean of residual (SRMR), the adjusted goodness of fit index (AGFI), the confirmatory fit index (CFI), the non-normed fit index or Tucker-Lewis Index (TLI), and the root mean-squared error of approximation (RMSEA). For the SRMR, value of <0.08, for the CFI and TLI, values of >0.95, for the AGFI, value of >0.90,32 and for the RMSEA measure, values of <0.0632 reflect adequate fits of a specified model to the data. The model fit for family support latent variable was acceptable, after allowing four error terms to correlate with each other (see Appendix, no. 2) to improve the model fit. $\chi^2 = 2.5$, BS $P = 0.11$; SRMR = 0.01; AGFI = 0.97; CFI = 0.997; TLI = 0.97; and RMSEA = 0.05. Factor loadings for the latent factor of family support for each of the five subscales were as follows: 0.85 (cohesion), 0.43 (expression), −0.64 (conflict), 0.57 (organization), and −0.14 (control), $P < 0.01$. Thus, a “supportive” family environment can be defined as a cohesive family relationship that encourages emotional expression with little conflict and an organized family system with little control.

The model testing for the rest of the latent variables as two-factor (i.e., intercept and slope) constructs revealed acceptable model fits: for the anxiety, multivariate kurtosis = 13.48, $P < 0.001$; $\chi^2 = 24.87$, BS $P = 0.17$; SRMR = 0.02; AGFI = 0.96; CFI = 0.98; TLI = 0.98; and RMSEA = 0.07; for the severity of post-treatment nausea, multivariate kurtosis = 8.41, $P < 0.001$; $\chi^2 = 25.96$, BS $P = 0.01$; SRMR = 0.02; AGFI = 0.96; CFI = 0.98; TLI = 0.98; and RMSEA = 0.07; and for the severity of anticipatory nausea, multivariate kurtosis = 45.49, $P < 0.001$; $\chi^2 = 29.74$, BS $P = 0.01$; SRMR = 0.03; AGFI = 0.94; CFI = 0.95; TLI = 0.96; and RMSEA = 0.08.

**Test of the Model Structure: Predicting the Severity of Anticipatory Nausea**

The fit of the proposed latent growth structural model including lagged effects was satisfactory: multivariate kurtosis = 104.37, $P < 0.001$; $\chi^2 = 137.29$, BS $P = 0.03$; SRMR = 0.03; AGFI = 0.94; CFI = 0.98; TLI = 0.98; and RMSEA = 0.03. We reported both regression weights, whose significance was tested using maximum likelihood standard errors, and total, direct, and indirect effects, whose significance was tested using bootstrap standard errors, in Table 2 and depicted in Fig. 2 for regression weights. Because of the difference in the way the standard errors of regression weights and effects were estimated (maximum likelihood vs. bootstrap), this resulted in differences in significance levels (Table 2). We made our interpretation based on regression weights. As shown in Table 2 and Fig. 2, hypothesis (a), the effect of post-treatment nausea on anticipatory nausea, was supported by the impact of the initial level of post-treatment nausea severity on an increase in the severity of anticipatory nausea ($\beta = 0.54$) and by the impact of the increase of post-treatment nausea severity on both the initial level ($\beta = 0.72$) and increase ($\beta = 0.52$) of anticipatory nausea severity.31,32

Hypothesis (b) regarding the direct effect of a patient’s anxiety on the development of anticipatory nausea was supported by the impact of the increase of anxiety on the initial severity level of anticipatory nausea ($\beta = 0.82$). The hypothesis (c) of the effect of a patient’s anxiety on the development of anticipatory nausea mediated by post-treatment nausea was supported for changes of latent variables, supporting the conditioning effect. The effect of initial anxiety level on the development of anticipatory nausea was mediated by the initial level of post-treatment nausea ($\beta = 0.26$), which in turn was associated with a greater increase in anticipatory nausea symptoms ($\beta = 0.54$). The indirect effects of anxiety on the initial level and the change of anticipatory nausea, however, were not significant (see Table 2, under “Indirect” column). In addition, a greater increase of patient’s anxiety was associated with a less increase of post-treatment nausea symptoms ($\beta = -0.53$), which in turn was associated with both a more severe initial level of anticipatory nausea ($\beta = 0.72$) and a greater increase in anticipatory nausea symptoms ($\beta = 0.52$).

Hypothesis (d), the effect of family support on anticipatory nausea mediated by anxiety, was not supported. The hypothesis (e) of an effect of family support on anticipatory nausea mediated by anxiety and post-treatment nausea was supported. The following three associations were significant: between family support and a patient’s level of anxiety ($\beta = -0.36$), between the level of anxiety and the level of severity of post-treatment nausea ($\beta = 0.26$),...
and between the level of severity of post-treatment nausea and the change of severity of anticipatory nausea ($\beta = 0.54$). Lack of supportive family is associated with a higher level of patient anxiety, which in turn, is associated with a more severe initial level of post-treatment nausea, which is then related to a greater increase in the anticipatory nausea symptoms. As reported in Table 2, the indirect effect of family support on the change of anticipatory nausea was significant.

The last hypothesis (f) that proposes the direct relationship between family support and anticipatory nausea confirms the initial severity level of anticipatory nausea ($\beta = -0.31$) but not the change of anticipatory nausea severity. A supportive family environment is associated with a less severe initial level of a patient’s anticipatory nausea; it is not associated with changes in severity of a patient’s anticipatory nausea across treatments (see Appendix, no. 3).

The cross-lagged effects among measures of anxiety, post-treatment nausea, and anticipatory nausea were significant only between anxiety at treatment one and the severity of anticipatory nausea at treatment two; and between the severity of post-treatment nausea at treatment one and the severity of anticipatory nausea at treatment two ($P < 0.05$). Finally, the emetic potential rating score of chemotherapy regimen for each patient was significantly

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### Table 2

<table>
<thead>
<tr>
<th>Latent growth structural effects</th>
<th>Regression Weight</th>
<th>Total Effect</th>
<th>Direct Effect</th>
<th>Indirect Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Support → Anxiety_Intercept</td>
<td>$-0.36^a$</td>
<td>$-0.36^a$</td>
<td>$-0.36^a$</td>
<td>—</td>
</tr>
<tr>
<td>Family Support → Anxiety_Slope</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>—</td>
</tr>
<tr>
<td>Family Support → ANS_Intercept</td>
<td>$-0.31^a$</td>
<td>$-0.24^b$</td>
<td>$-0.31$</td>
<td>0.07</td>
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<tr>
<td>Family Support → ANS_Slope</td>
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<td>$-0.01$</td>
<td>0.19</td>
<td>$-0.20^c$</td>
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<tr>
<td>Anxiety_Intercept → PNS_Intercept</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>—</td>
</tr>
<tr>
<td>Anxiety_Intercept → PNS_Slope</td>
<td>0.08</td>
<td>0.08</td>
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<td>—</td>
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<tr>
<td>Anxiety_Intercept → ANS_Intercept</td>
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<td>$-0.15$</td>
<td>$-0.20$</td>
<td>0.05</td>
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<tr>
<td>Anxiety_Intercept → ANS_Slope</td>
<td>0.38</td>
<td>0.56</td>
<td>0.38</td>
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<tr>
<td>Anxiety_Slope → PNS_Intercept</td>
<td>0.42</td>
<td>0.42</td>
<td>0.42</td>
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<tr>
<td>Anxiety_Slope → PNS_Slope</td>
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<td>$-0.53$</td>
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<td>—</td>
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<tr>
<td>Anxiety_Slope → ANS_Intercept</td>
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<td>0.42</td>
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<td>Anxiety_Slope → ANS_Slope</td>
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<td>$-0.04$</td>
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<tr>
<td>PNS_Intercept → ANS_Intercept</td>
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<td>$-0.05$</td>
<td>$-0.05$</td>
<td>—</td>
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<tr>
<td>PNS_Intercept → ANS_Slope</td>
<td>0.54</td>
<td>0.54</td>
<td>0.54</td>
<td>—</td>
</tr>
<tr>
<td>PNS_Slope → ANS_Intercept</td>
<td>0.72</td>
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</tr>
<tr>
<td>PNS_Slope → ANS_Slope</td>
<td>0.52</td>
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<td>—</td>
</tr>
<tr>
<td>Emetic Score → PNS_Intercept</td>
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<tr>
<td>Emetic Score → PNS_Slope</td>
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<td>Emetic Score → ANS_Intercept</td>
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<td>0.07</td>
<td>0.18</td>
<td>$-0.11$</td>
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<td>Emetic Score → ANS_Slope</td>
<td>0.07</td>
<td>0.05</td>
<td>0.07</td>
<td>$-0.02$</td>
</tr>
</tbody>
</table>

### Lagged Effects

| Anxiety_T1 → PNS_T2 | 0.03 | 0.03 | 0.03 | — |
| Anxiety_T2 → PNS_T3 | 0.02 | 0.02 | 0.02 | — |
| Anxiety_T3 → PNS_T4 | $-0.01$ | $-0.01$ | $-0.01$ | — |
| Anxiety_T4 → PNS_T5 | 0.03 | 0.03 | 0.03 | — |
| Anxiety_T1 → ANS_T2 | 0.14 | 0.14 | 0.14 | 0.00 |
| Anxiety_T2 → ANS_T3 | 0.08 | 0.08 | 0.08 | 0.00 |
| Anxiety_T3 → ANS_T4 | 0.00 | 0.00 | 0.00 | 0.00 |
| Anxiety_T4 → ANS_T5 | 0.01 | 0.01 | 0.01 | 0.00 |
| PNS_T1 → ANS_T2 | 0.16 | 0.16 | 0.16 | — |
| PNS_T2 → ANS_T3 | 0.08 | 0.08 | 0.08 | — |
| PNS_T3 → ANS_T4 | 0.04 | 0.04 | 0.04 | — |
| PNS_T4 → ANS_T5 | $-0.02$ | $-0.02$ | $-0.02$ | — |

$^a$: $P < 0.001$.

$^b$: $P < 0.01$.

$^c$: $P < 0.05$.

PNS = Post-treatment Nausea Severity; ANS = Anticipatory Nausea Severity. Maximum Likelihood standard error (SE) was used to test significance of regression weights; bootstrap SE was used to test significance of total, direct, and indirect effects.
related to only the initial severity level of post-treatment nausea but was not significantly related to the initial severity level of anticipatory nausea or changes of both types of nausea.

In summary, the results indicate that a supportive family environment is associated with the severity of anticipatory nausea being mediated by lower levels of patient anxiety and severity of post-treatment nausea, or directly being associated with a less severe level of anticipatory nausea symptoms.

**Discussion**

This study examined the effects of family support and anxiety on the development of a patient’s anticipatory nausea during chemotherapy treatment. Two major findings suggest that family environment influences the development of patient anticipatory nausea. First, supportive family environment was related to a less severe level of patient anticipatory nausea, directly. Second, supportive family environment was related to less increase in the severity of anticipatory nausea symptoms mediated by lowering the patient’s anxiety and severity of post-treatment nausea. These effects of family support were independent of the effect of emetic drugs on symptoms of chemotherapy-related nausea.

Specifically, the results in the present study revealed that the association between family support and the rate of change in severity of anticipatory nausea was mediated by the initial level of patient anxiety and actual symptoms of nausea after the first chemotherapy treatment. Each association among these factors has been found separately in previous empirical studies, but none of these studies has examined the associations among the factors in a simultaneous and longitudinal model. The results in the present study also showed that family environment had a direct impact on a patient’s symptoms of anticipatory nausea due to chemotherapy treatment for cancer, above and beyond the impact of the patient’s anxiety and symptoms of post-treatment nausea.

The current findings are conceptually consistent with Holahan and Moos’ study, which demonstrated that an unbalanced or disruptive family environment increased psychosomatic complaints from family members in nonpatient population. The findings are also consistent with existing empirical studies on a patient’s physical adjustment to cancer. In addition, the findings highlight the unique contribution of family support to a patient’s adjustment for cancer treatment, because the impact of family support on the degree to which a patient develops anticipatory nausea was clear even in the context of hypothesized mediators in a model using structural equation modeling.

The present study helps to clarify the dynamics among predictors of the development of anticipatory nausea using a latent growth structural model, including cross-lagged effects of the variables. Our study illustrates that the association between supportive family environment and the severity of anticipatory nausea is cross-sectional that has attenuated carryover effect to symptoms at later treatments (see Appendix, no. 4). The increase of anticipatory nausea severity is better predicted by the indirect effects of family support through reducing initial levels of the patient’s anxiety and post-treatment nausea severity. It seems that the beneficial effects of supportive family environment on reducing anxiety and symptoms of chemotherapy-related nausea are stable across treatments.

A study of patients with Hodgkin’s disease found that those who reported developing anticipatory symptoms during their cancer treatment were more likely to continue to experience difficulties during the post-treatment period. Our results further suggest that it will be helpful to identify patients whose familial environment is lack of support, at the beginning of a course of chemotherapy treatment before the patients develop conditioned responses to the treatments. The object of this process of identification is to prevent any detrimental impact on the patient’s adjustment to treatment during the course of chemotherapy treatment, or even long after treatments end. The findings suggest that at an early stage of treatment, helping patients and their families communicate in more satisfactory and supportive ways, and maintaining an organized family system, might be beneficial in reducing the patient’s anxiety and chemotherapy-related nausea during cancer treatment.

The finding that a supportive family environment contributed significantly to a patient’s well-being, even when potential pharmacological impact on nausea was controlled, suggests
that nonpharmacological or psychological factors play a significant role in inhibiting development of chemotherapy-induced nausea. This finding is consistent with empirical studies\(^5\) and a meta-analysis on the effects of psychosocial interventions on adult cancer patients’ adjustment.\(^34\)

**Limitations**

Limitations of this study should also be addressed. First, only the patients’ perceptions of their family environment were assessed. Although patients’ perceptions are probably the key ones to include in the model, family dynamics are reciprocal between patients and their family members;\(^35\) thus, both the patient’s and the family members’ perceptions about adjustment need to be included in future studies. Second, all measures used in the present study were patient’s self-report; thus there may be a potential issue of response bias. Third, because each questionnaire packet was given to the subject to complete at home and to be returned in a week, the assessments for anxiety and nausea were retrospective and the actual time that questionnaires were answered was not available. Although this weakness in study design was compensated for statistically by testing the cross-lagged effects of anxiety on anticipatory nausea, obtaining a patient’s anxiety level before getting a treatment would be ideal to control for any potential artifact.

It can be also speculated that our nonsignificant findings might be due to nonlinear (quadratic or cubic) trends in variables. Because we did not have a theory about pure nonlinear trends in variables and the nonlinear components might exist in addition to, but not instead of, linear trend, it is unlikely that our nonsignificant findings become significant when we use higher-order trends. The nonlinear trends need to be tested with more time points in future studies. Finally, the findings in the present study need cautious interpretation when applied to cancer populations other than female breast cancer patients.

**Future Directions and Conclusion**

In the present study, the initial level of a patient’s anxiety mediated the impact of family support on the initial level of post-treatment nausea severity, whereas it did not mediate the effects of family support on the development of anticipatory nausea severity (although it did so via the post-treatment nausea severity). These findings about the different roles of family support and a patient’s anxiety on the two types of highly related chemotherapy-induced nausea need to be replicated with heterogeneous populations. In addition, future studies will be needed to examine more refined mechanisms to decipher the effect of family support on a patient’s symptoms of anticipatory nausea. Encouraging patients and families to express feelings openly, avoid conflict, and maintain a balanced family structure may prove beneficial for their adjustment to cancer.
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References


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Appendix

1. These 12 patients were not significantly different in study variables. Including the 12 patients did not make any significant changes in the subsequent analyses. In addition, the initial levels of anxiety, severity of post-treatment nausea, and severity of anticipatory nausea by the 29 participating hospitals were not significantly different across the 29 participating hospitals: intraclass correlation coefficients = 0.02, 0.03, 0.02, Ps > 0.27, respectively.

2. Four error terms between expression and organization, expression and control, conflict and control, and organization and control were allowed to correlate. The inclusion of the correlated error terms changed factor loadings slightly (the changes ranged from 0 to 0.04), and each of the five factor loadings were significant regardless of these correlated error terms.

3. We also tested three paths that might involve opposite direction. The new three paths were paths from intercept of post-treatment nausea to slope of anxiety; from intercept of anticipatory nausea to slope of anxiety; and from intercept of anticipatory nausea to slope of post-treatment nausea. A new model replacing these three paths fits the data satisfactorily: multivariate kurtosis = 104.37, P < 0.001; \( \chi^2_{(150)} = 222.75 \), BS \( P = 0.01 \); SRMR = 0.04; AGFI = 0.94; CFI = 0.98; TLI = 0.97; and RMSEA = 0.04, but is worse than the original study model. Among the new three paths, only the path from intercept of post-treatment nausea to slope of anxiety was significant (\( P < 0.01 \)), but the other two paths were not significant (\( P > 0.78 \)). In addition, paths from post-treatment nausea latent variables to anticipatory nausea latent variables became nonsignificant, whereas the paths from family support to intercept of anxiety, from family support to intercept of anticipatory nausea, from intercept of anxiety to intercept of post-treatment nausea, and from slope of anxiety to slope of post-treatment nausea remained significant; and the path from family support to slope of anticipatory nausea became significant.

4. To test if the effect of family support on the development of anticipatory nausea is stable over time, we re-specified the intercepts of latent variables to refer to different treatments such as fixing study slope loadings to −1, 0, 1, 2, and 3 for referring to treatment 2; to −2, −1, 0, 1, and 2 for referring to treatment 3, and so forth. The results showed that the associations between family support and the intercept of anxiety across different treatments remained significant (−0.35 < regression weights < −0.33, Ps < 0.001), whereas the associations between family support and the intercept of anticipatory nausea became weaker as the treatment proceeded (regression weights = −0.20, \( P < 0.001 \); −0.13, \( P < 0.05 \); and −0.07, non-significant, for treatments 3 to 5). Other associations between family support and slope of either anxiety or anticipatory nausea remained nonsignificant (regression weights ranged from 0.04 to 0.06 and 0.15 to 0.16, respectively).