

Modeling Causes of Aggressive Behavior in Patients With Dementia

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Purpose of the Study: To examine factors predicting development of aggression in patients with dementia as a step toward developing preventive strategies and nonpharmacologic therapies. **Design and Methods:** Study participants were 171 nonaggressive, community-residing VA patients aged more than 60, newly diagnosed with dementia. Patients and caregivers were assessed at baseline and at months 5, 9, 13, 17, 21, and 25. Aggression was evaluated using the Cohen-Mansfield Agitation Inventory. Survival models incorporating direct and indirect effects were conducted to estimate associations between psychosocial factors (baseline and change measures of dementia severity, pain, depression, caregiver burden, patient-caregiver relationship, and nonaggressive physical agitation) and time to aggression onset. **Results:** Higher levels of baseline caregiver burden, worst pain, declining patient-caregiver relationship, and increasing nonaggressive physical agitation predicted increased risk of aggression. Baseline dementia severity and depression were indirectly related to onset of

aggression. The association between increasing nonaggressive physical agitation and time to aggression onset was independent of the associations between our psychosocial measures and time to aggression onset. **Implications:** Potentially mutable factors were associated with development of aggression. The longitudinal design of this study and its sample of newly diagnosed, previously nonaggressive dementia patients strengthen prior findings in the literature.

Key Words: *Structural equation models, Veterans*

Aggressive behavior is among the most distressing and dangerous of symptoms experienced by individuals with dementia (Chappell & Penning, 1996). Aggression presents a serious challenge for caregivers, possibly placing them at risk for harm, and increasing the risk of psychotropic medication use and nursing home placement (Kunik et al., 2010a). Aggression is defined as any physical or verbal behavior that has the effect of harming or

repelling others and includes behaviors such as hitting, kicking, and verbal threats (Ryden, 1988). Approximately 40% of patients diagnosed with dementia ultimately exhibit aggressive behavior (Kunik et al., 2010b).

Longitudinal studies of aggression have found incidence rates ranging from 10% to 31%, primarily due to varying definitions of aggression and frequently failing to distinguish between aggression and nonaggressive agitation with the two often combined into a single assessed measure of agitation/aggression (Cohen-Mansfield, Marx, & Rosenthal, 1989; Cummings et al., 1994; Kunik et al., 2010b). The onset of aggression appears to be a consequence of complex interrelations between various biologic, psychosocial, caregiving, and environmental factors in patients with dementia (Bird, 2010). Depression, psychosis, pain, caregiver burden, quality of caregiver–patient relationship and social and environmental stimulants have been associated with aggression (Cohen-Mansfield & Werner, 1998b). Our own previously published causal model of the development of aggression among nonaggressive patients newly diagnosed with dementia predicts that aggression results from a combination of internal factors (i.e., characteristics or experiences of the person with dementia) that include depression, pain, psychosis, dementia severity, and external factors (i.e., conditions existing outside of the person with dementia) that include caregiver burden and the quality of the patient–caregiver relationship (Kunik et al., 2003, 2010b).

Nonaggressive physical agitation is also a potentially important factor in the development of aggression. Agitation, in general, is a symptom of dementia and is defined as inappropriate verbal, vocal, or motor activity resulting from needs and confusion of the agitated individual (Cohen-Mansfield, 2009; Cohen-Mansfield & Werner, 1998a). Agitation can manifest as aggressive or nonaggressive, with nonaggressive agitation defined as excessive verbal and/or motor behavior that may or may not escalate to aggression (Cohen-Mansfield, 1986).

Studies have found that depression, psychosis, severe cognitive impairment, poor physical health, and reduction in environmental stimuli are associated with both physical and verbal agitation (Cohen-Mansfield & Werner, 1998b; Kunik et al., 1999). Predictors of agitation include pain, and psychological needs (e.g., hunger, thirst, excretion,

and sleep) as well as disruption of familiar routines, absence of familiar people, lack of participation in activities, and overstimulation (Kunik et al., 2003).

There is surprisingly little literature examining whether nonaggressive agitation is predictive of the development of aggression (Aarsland, Cummings, Yenner, & Miller, 1996; Gormley, Rizwan, & Lovestone, 1998). To demonstrate a predictive relationship, it is necessary to clearly distinguish between the two. Agitation includes behaviors such as wandering and increased psychomotor activity, which often do not require intervention. Conversely, aggression includes verbal or physical actions intended to harm and almost always requires intervention (Kunik et al., 2010b).

In our prior work, we examined measures of intrinsic and extrinsic factors for their ability to predict time to onset of aggression. These included measures of depression, psychosis, and pain as intrinsic factors, and caregiver burden, quality of the patient–caregiver relationship (mutuality), and social stimulation as extrinsic factors. For all measures, we included both baseline measures and measures of change over time in our models (Kunik et al., 2010b). Our models showed that higher baseline levels of caregiver burden and pain, and decline in patient–caregiver mutuality over time, were jointly associated with increased risk of aggression (as distinct from nonaggressive agitation) in patients with newly diagnosed dementia. The other measures of intrinsic and extrinsic factors, both baseline and change measures, were not statistically significant as predictors of time to onset of aggression. Our findings further suggested that the association between patient depression and time to onset of aggression, may be indirect and mediated by patient-reported pain, caregiver burden, and change in patient–caregiver mutuality (Kunik et al., 2010b). We did not explicitly test this possible mediation. We have shown in other analyses on these data that reported pain is associated with subsequent increases in patient depression and might be associated with increases in nonaggressive agitation (Snow et al., 2009).

Although we carefully distinguished between aggression and nonaggressive agitation in our prior work, we did not test the association between the two. Agitation has been linked in previous studies to some of the factors included in our prior work, for example, depression (Kunik et al., 1999; Levy et al., 1996), pain (Zieber, Hagen,

Armstrong-Esther, & Aho, 2005), and cognitive impairment (Cohen-Mansfield & Werner, 1998a; Levy et al., 1996), although evidence is inconsistent. Because nonaggressive agitation and aggression have not been consistently distinguished in the literature, it is unclear what the pattern of relationships is between our psychosocial measures, nonaggressive agitation, and the time to aggression onset.

In these analyses, we build on our prior work on the psychosocial predictors of aggression to examine potential direct and indirect relationships between aggression and factors posited by our predictive model. Starting with the measures identified in our prior analyses as potentially directly or indirectly related to time to onset of aggression, we explicitly examine (a) whether the relationships between depression, dementia severity, and the time to aggression onset were mediated by caregiver burden and the quality of the patient-caregiver relationship, as implied by our earlier work; (b) whether the psychosocial factors that predicted the time to aggression onset, directly or indirectly, in our prior analyses (pain, caregiver burden, change in patient-caregiver mutuality, dementia severity, and depression) were also associated with nonaggressive physical agitation; (c) whether nonaggressive agitation was predictive of time to aggression onset; and (d) whether nonaggressive agitation mediated any of the relationships between time to aggression onset and the psychosocial factors identified in our earlier model.

Methods

Study Population

This study was a part of a larger longitudinal study of causes and consequences of aggression in patients with dementia. Study methods have been described elsewhere (Kunik et al., 2010b). Briefly, newly diagnosed, nonaggressive patients with dementia were identified through the Veterans Administration Outpatient Data files, flyers, radio, and print advertisements and the Michael E. DeBakey Veterans Affairs (VA) Medical Center primary care and geriatrics clinics. A letter was sent to eligible participants diagnosed with dementia during 2001–2004. Patients with a prior diagnosis of aggression who resided in a nursing home or had a caregiver present less than 8 hr per week were excluded. The final sample was largely men, reflecting the patient demographics at the Michael E. DeBakey VA Medical Center (Table 1).

Inclusion/Exclusion Criteria

Inclusion criteria were age more than 60 years and new diagnosis of dementia, defined as receiving an initial outpatient *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) code for dementia (290.XX, 291.2, 292.82, 294.1, 294.8, or 331.0) within 12 months before screening, with no other dementia codes recorded for 2 preceding years. Exclusion criteria were (a) aggressive behavior in the past year, (b) current residence in a nursing home, or (c) having a caregiver less than 8 hr per week. Dementia diagnoses were confirmed through medical records and caregiver report. Potential participants subsequently underwent telephone screening to verify eligibility criteria. Aggressive patients were excluded using three probes from the Ryden Aggression Scale (Ryden, 1988) regarding (a) unprovoked deliberately unfriendly or violent behavior, including hitting, pushing and/or throwing things, cursing a person, calling people names, and using hostile and/or accusatory language; (b) physical aggression such as hitting, pushing, or throwing things that caused physical injury to the patient, caregiver, or others; or (c) verbal aggression, such as making verbal threats to hurt people, cursing people, or accusing people of doing things, in a hostile manner. Once participants were enrolled, the full Ryden scale was used to confirm that aggressive behaviors had not been present during the previous year.

This research was approved by the Houston VA Research and Development Committee and the Baylor College of Medicine Institutional Review Board.

Study Design and Variable Measurement

A longitudinal study design was employed. Patients and caregivers were assessed over 24 months starting at baseline and then at months 5, 9, 13, 17, 21, and 25.

Aggression and Agitation.—Aggression (the study outcome) was evaluated using the Cohen-Mansfield Agitation Inventory (CMAI) aggression subscale, which relies on a 7-point Likert scale for frequency and a 5-point Likert scale for disruptiveness (O'Malley, Orengo, Kunik, Snow, & Molinari, 2002; Shahar, Snow, Soucek, Ashton, & Kunik, 2004). Aggression was considered present if a participant scored over zero on both frequency and disruptiveness on the total aggression subscale, comprising any of the 13 questions referring to

intent to harm through spitting, verbal aggression, hitting, kicking, grabbing, pushing, throwing, biting, scratching, hurting self/others, tearing things/destroying property, making inappropriate verbal sexual advances, or making inappropriate physical sexual advances.

Nonaggressive agitation was evaluated using the physical, nonaggressive agitation subscale of the CMAI, for example, Pacing and aimless wandering, repetitious mannerisms, general restlessness, or hiding, or hoarding things (Cohen-Mansfield, 2009). We evaluated both our baseline measure of agitation and change in agitation over the study period.

Dementia severity was assessed using the Dementia Rating Scale (DemRS2). The Dementia Rating Scale has been shown to have adequate internal consistency (split-half $r = .90$), test-retest reliability ($r = .97$) and convergent and predictive validity (Jurica, Leitten, & Mattis, 2001). For these analyses, we used the DRS2 age- and education-corrected scaled scores from Mayo's Older Americans Normative Studies. These scores range from 2 to 18, with lower scores representing greater impairment (Jurica et al., 2001).

Depression was assessed using the Hamilton Rating Scale for Depression (HAM-D). It is both valid and reliable for older adults with depression, including those with dementia. With the adapted HAM-D, the clinical rater combines information from observations with an interview of both patient and caregiver. Possible scores ranged from 0 to 68 (10–13, mild depression; 14–17, mild-to-moderate depression; and >17, moderate-to-severe depression) (Hamilton, 1967). Interrater reliability on the HAM-D is typically high ($>.84$; McDowell, 2006).

Worst pain was measured using the “worst pain” item from the Philadelphia Geriatric Center Pain Intensity Scale (Cronbach's $\alpha = .84$ for the scale as a whole) that assesses the highest level of pain experienced over the preceding 4 weeks on a 5-point scale (1 = not at all, 2 = a little, 3 = some, 4 = quite a bit, and 5 = a great deal; Parmelee, Katz, & Lawton, 1991; Parmelee, Smith, & Katz, 1993).

The nature of the relationship between the person with dementia and his/her primary caregiver was assessed in two ways. First the quality of the *patient-caregiver relationship* was evaluated using the Mutuality Scale, which has been used in patients with Alzheimer's disease (Archbold & Stewart, 1986; Gallagher-Thompson, Dal Canto, Jacob, & Thompson, 2001). The Mutuality Scale (Archbold & Stewart, 1986) measures the positive quality of the relationship between a family

caregiver and care receiver and is composed of 15 items describing the frequency (0 = not at all, 1 = a little, 2 = some, 3 = quite a bit, and 4 = a great deal) of communication, positive engaging interactions, attachment, and emotional support. The score consists of the sum of the frequencies (0–60) and has good internal consistency (Cronbach's $\alpha = .91$) and test-retest reliability ($r = .79$). The total mutuality score representing the average of all items was used in the analyses (Archbold, Stewart, Greenlick, & Harvath, 1990). Second, *caregiver burden* was determined using the Burden Interview, which measures the perceived impact of caregiving on the caregiver's financial/physical status, physical/emotional health, and social activities using a 22-question Likert scale questionnaire with five options, from zero to four. Range of scores is 0–88 (0–20, little or no burden; 21–40, mild-to-moderate burden; 41–60, moderate-to-severe burden; and 61–88, severe burden). The scale has established reliability (Cronbach's $\alpha = .92$) and validity and is specifically utilized in patients with dementia (Hérbert, Bravo, & Prévile, 2000; Zarit, Anthony, & Boutselis, 1987).

Participants and their caregivers were followed for 24 months. All assessments were conducted during home visits at baseline and at 4-month intervals. A positive finding of onset of aggressive behavior terminated the home visits and the collection of the psychosocial measures.

Data Analyses

Mediation is implied when the relationship between a predictor and outcome measure is accounted for wholly or in part by a second variable that is related to both the predictor and outcome (Baron & Kenny, 1986; Muller, Judd, & Yzerbyt, 2005). For these analyses, our outcome variable was time to aggression onset. For our predictive measures, we estimated the change over time between each participant's baseline observation and last available observation by calculating the linear slope of change across all available study observations for each individual. Because multiple observations are necessary to calculate change, only participants with two or more observations were included in our analyses. As a result, all participants who had aggression onset before the first follow-up at 5 months (as determined during the first follow-up visit) were excluded, because the onset of aggressive behavior terminated the home visits and the collection of the psychosocial

measures. All change estimates were scaled to represent change over 12 months. Change was not estimated for dementia severity because it was only assessed at baseline.

We fit survival models examining the associations between baseline nonaggressive physical agitation, dementia severity, depression, pain, caregiver burden, change in mutuality, and change in nonaggressive physical agitation and the time to aggression onset within a path analytic framework using MPlus Version 5.21 (MPlus, 2012; Muthen & Muthen, 1998–2009). Survival models can be treated as a specific case of the more general class of latent variable models (Asparouhov, Masyn, & Muthen, 2006). MPlus enables the estimation of direct and indirect relationships within a path analysis framework by allowing the simultaneous estimation of regression and survival model components. The inputs for our models were the observed baseline measures of our psychosocial variables and our measure of nonaggressive physical agitation, and the separately estimated change measures for patient–caregiver mutuality and nonaggressive physical agitation (described previously). All of our baseline predictive measures and measures of estimated change were treated as continuous. Time to aggression onset was treated as a continuous time to event variable. The correlations among our predictive measures were also estimated using MPlus.

Model parameters were estimated using the method of maximum likelihood with robust standard error estimation (Muthen & Muthen, 1998–2009). Model fit was evaluated with the Akaike Information Criterion (AIC); a smaller AIC indicates a better fit. The Bayesian Information Criterion (BIC) and the adjusted BIC were also used as tests of model fit. The AIC and BIC are not absolute measures but are used to compare the fit of two or more models estimated from the same data set. The chi-square test based on the discrepancy between the sample and fitted covariance matrices was used as a conventional overall test of fit.

Results

Descriptive Statistics

A total of 215 newly diagnosed nonaggressive dementia patients who consented to participate were enrolled in the study. Patients who were determined to have had an onset of aggression between the baseline assessment and the first follow-up visit

Table 1. Participant Demographics and Study Variable Baseline Values ($n = 171$)

| Variable | Value |
|----------------------------------------------|---------------|
| Sample characteristics | |
| Men (n , %) | 161 (94.44) |
| Age (mean, SD) | 75.81 (6.19) |
| White (n , %) | 99 (78.57) |
| Black (n , %) | 25 (19.84) |
| Other (n , %) | 2 (1.59) |
| Baseline measures in model | |
| Dementia severity (mean, SD) | 4.12 (2.79) |
| Depression (mean, SD) | 6.16 (5.28) |
| Burden (mean, SD) | 14.73 (12.21) |
| Worst pain (mean, SD) | 1.91 (1.53) |
| Nonaggressive physical agitation (mean, SD) | 12.14 (4.50) |
| Change measures in model | |
| Change in mutuality (mean, SD) | -.27 (0.77) |
| Change in nonaggressive agitation (mean, SD) | .08 (4.85) |

Note: Dementia Severity = Dementia Rating Scale; Depression = Hamilton Rating Scale for Depression; Worst Pain = Item from Philadelphia Geriatric Center Pain Intensity Scale.

at 5 months and patients with insufficient baseline data were excluded from the analyses, resulting in a final sample of 171 patients. Participant demographic data and baseline levels of the predictors are presented in Table 1. A majority of the patients (94%) were men. Mean age of the participants was approximately 76 years ($SD = 6.04$), with a range of 60–90 years. Most patients were married. Approximately 79% of the participants were White, and almost all the rest (about 20%) were African Americans. Thirty-eight percent (65 of 171) of the final sample developed aggression during the follow-up period.

Analysis Results

The correlations among our predictive measures are shown in Table 2. Our earlier work showed that both our measure of depression and of dementia severity at baseline were separately related to time to onset of aggression, but became nonsignificant when included in a model with baseline measures of caregiver burden and worst pain, and our measure of change in patient–caregiver mutuality (Kunik et al., 2010b). In order to test whether the relationships between dementia severity and depression were mediated by the psychosocial predictors that emerged from our earlier analyses, we constructed a full model testing the direct and the indirect paths among our psychosocial measures and the time to aggression onset. A reduced model was constructed

Table 2. Correlations Among the Model Predictors ($n = 171$)

| Predictor | Dementia severity | Burden | Worst pain | Change in mutuality | Depression | Agitation ^a |
|----------------------------------|-------------------|--------|------------|---------------------|------------|------------------------|
| Burden | -.23*** | — | | | | |
| Worst pain | .12 | -.05 | — | | | |
| Change in mutuality | .01 | -.01 | -.14* | — | | |
| Depression | .03 | .17* | .30 | -.10 | — | |
| Agitation ^a | -.19*** | .39*** | .06 | .01 | .12* | — |
| Change in agitation ^a | -.05 | -.10 | -.05 | .05 | -.06 | -.23 [†] |

^aNonaggressive physical agitation.

Statistical significance: [†] $\leq .10$, * $\leq .05$, ** $\leq .01$, *** $\leq .001$.

Table 3. Model Results: Time to Aggression Onset

| | Time to aggression onset | |
|----------------------------------|-----------------------------------------|-----------------------------------------|
| | Model 1 (no agitation) | Model 2 (with agitation) |
| | β (SE) ^a | β (SE) ^a |
| Survival component | | |
| Dementia severity | -.023 (0.13) [†] | -.017 (0.10) [†] |
| Caregiver burden | 0.70 (0.13)*** | 0.66 (0.10)*** |
| Worst pain | 0.47 (0.13)*** | 0.38 (0.13)** |
| Change in mutuality | -.039 (0.15)** | -.042 (0.11)*** |
| Change in agitation | — ^b | 0.45 (0.09)** |
| Regression components | | |
| | <i>Caregiver burden</i> | <i>Caregiver burden</i> |
| Dementia severity | -.017 (0.05)*** | -.012 (0.05)* |
| Depression | 0.13 (0.06)* | .10 (0.06) [†] |
| Nonaggressive physical agitation | — ^b | .35 (0.08)*** |
| | <i>Worst pain</i> | <i>Worst pain</i> |
| Depression | .22 (0.05)*** | .22 (0.05)*** |
| | <i>Nonaggressive physical agitation</i> | <i>Nonaggressive physical agitation</i> |
| Dementia severity | — ^b | -.014 (0.04)*** |
| Depression | — ^b | 0.09 (0.04)* |
| | <i>Change in agitation</i> | <i>Change in agitation</i> |
| Nonaggressive physical agitation | — ^b | -.023 (0.14) [†] |
| Model fit | | |
| Log likelihood | -3482.12 | -3454.99 |
| AIC | 7006.24 | 6961.98 |
| BIC | 7072.21 | 7043.66 |
| Adjusted BIC | 7005.72 | 6961.34 |

Note: AIC = Akaike Information Criterion; BIC = Bayesian information criterion.

^aStandardized coefficients.

^bNot estimated.

Statistical Significance: [†] $\leq .10$, * $\leq .05$, ** $\leq .01$, *** $\leq .001$.

by sequentially removing nonsignificant paths and reevaluating model fit until only statistically significant predictive paths remained ($p < .10$). Table 3 (Model 1) presents the resulting model. As we had previously demonstrated (Kunik et al., 2010b), higher levels of baseline caregiver burden ($p \leq .001$), worst pain over 4 weeks ($p \leq .001$), and decline in mutuality over time ($p \leq .01$) were significant predictors of increased risk of aggression

in patients suffering from dementia. The relationship between depression and the time to aggression onset appeared to be mediated by pain ($p \leq .001$) and caregiver burden ($p \leq .02$), whereas the relationship between baseline dementia severity and the time to aggression onset appeared partially mediated by caregiver burden ($p \leq .001$ with dementia severity), although the direct relationship between dementia severity and time to aggression onset remained

marginally significant ($p \leq .09$). Although not shown in Table 3, there were no significant correlations among our exogenous predictors.

We next estimated the associations between time to aggression onset and our baseline measure of nonaggressive physical agitation and change in nonaggressive physical agitation. Both baseline physical agitation (β [SE] = .89 [.10], $p \leq .001$) and change in physical agitation (.71 [.14], $p \leq .001$) significantly predicted the time to aggression onset. When they were added to Model 1 (described previously), baseline nonaggressive physical agitation became nonsignificant, whereas change in agitation remained significant. We repeated the process described previously to test the indirect paths between our agitation measures and time to aggression onset.

In general, the relationships shown in Model 1 did not change, with the exception that the direct relationships for both dementia severity and depression with caregiver burden were weakened slightly. In Model 2, both depression and dementia severity were also indirectly related to caregiver burden through their relationships with our baseline measure of agitation ($p \leq .03$ with depression and $p \leq .001$ with dementia severity). Notably, change in agitation was not related to any of the psychosocial measures in the model, suggesting that their respective influences on the time to aggression onset were independent. In contrast, the relationship between baseline nonaggressive physical agitation and time to aggression onset appeared mediated by caregiver burden ($p \leq .001$), and to a lesser extent change in nonaggressive physical agitation ($p \leq .10$).

As with Model 1, there were no significant correlations among our exogenous predictors. Our final model (Model 2) combining both our psychosocial predictors and our measures of agitation is shown in Figure 1.

Discussion

The purpose of the study was to investigate both direct and mediated relationships between our predictors and the onset of aggression. This approach extends and strengthens our prior findings, in particular by highlighting the contribution of increasing nonaggressive physical agitation toward the development of aggression.

This is the first longitudinal study to examine both direct and indirect relationships between psychosocial factors (dementia severity, pain,

depression, caregiver burden, patient–caregiver mutuality, and nonaggressive physical agitation) and time to aggression onset. Previous studies have demonstrated associations between aggression and psychosocial factors. However, our study results go beyond association to examine the nature of the casual relationship, suggesting indirect relations between dementia severity, depression, and the time to aggression onset that are mediated by other factors such as pain and caregiver burden. Interestingly, in our analyses change in nonaggressive physical agitation predicts the time to aggression onset independently from our psychosocial predictors. In contrast, our baseline measure of nonaggressive physical agitation is directly related to our baseline measures of dementia severity and depression, and indirectly related to aggression onset, primarily through caregiver burden. Thus, agitation’s role as a mediator for the psychosocial measures in predicting aggression is only partially supported by our findings.

Our longitudinal study design, standardized repeated measures, sample of newly diagnosed patients with dementia and use of a survival analytic approach incorporating direct and indirect effects are some of the major strengths of the study. However, there are also some limitations. First, because the study sample was composed of veterans, it was predominantly men due to the predominance of men in the U.S. military. Second, we did not differentiate between types of dementia, because the diagnoses were performed by primary care physicians who often do not specify the type (Krishnan et al., 2005). Third, other intrinsic and extrinsic factors that can lead to the development of aggression such as anxiety and physical impairment were not measured in this study. Finally, mediation analyses as described by Baron and Kenny (1986) assume the absence of measurement error in the mediating variables. That was not the case in these data. However, such measurement error will generally reduce the mediating effect of the intervening measure. Thus, our estimates of mediation are probably understated. Future work should incorporate multiple indicators of relevant predictive factors to help in reducing the impact of measurement error.

This study results have important preventive and treatment implications for the almost 40% of patients suffering from dementia that exhibit aggressive behavior each year. The psychosocial factors we found to be directly or indirectly related to time to aggression onset (agitation,

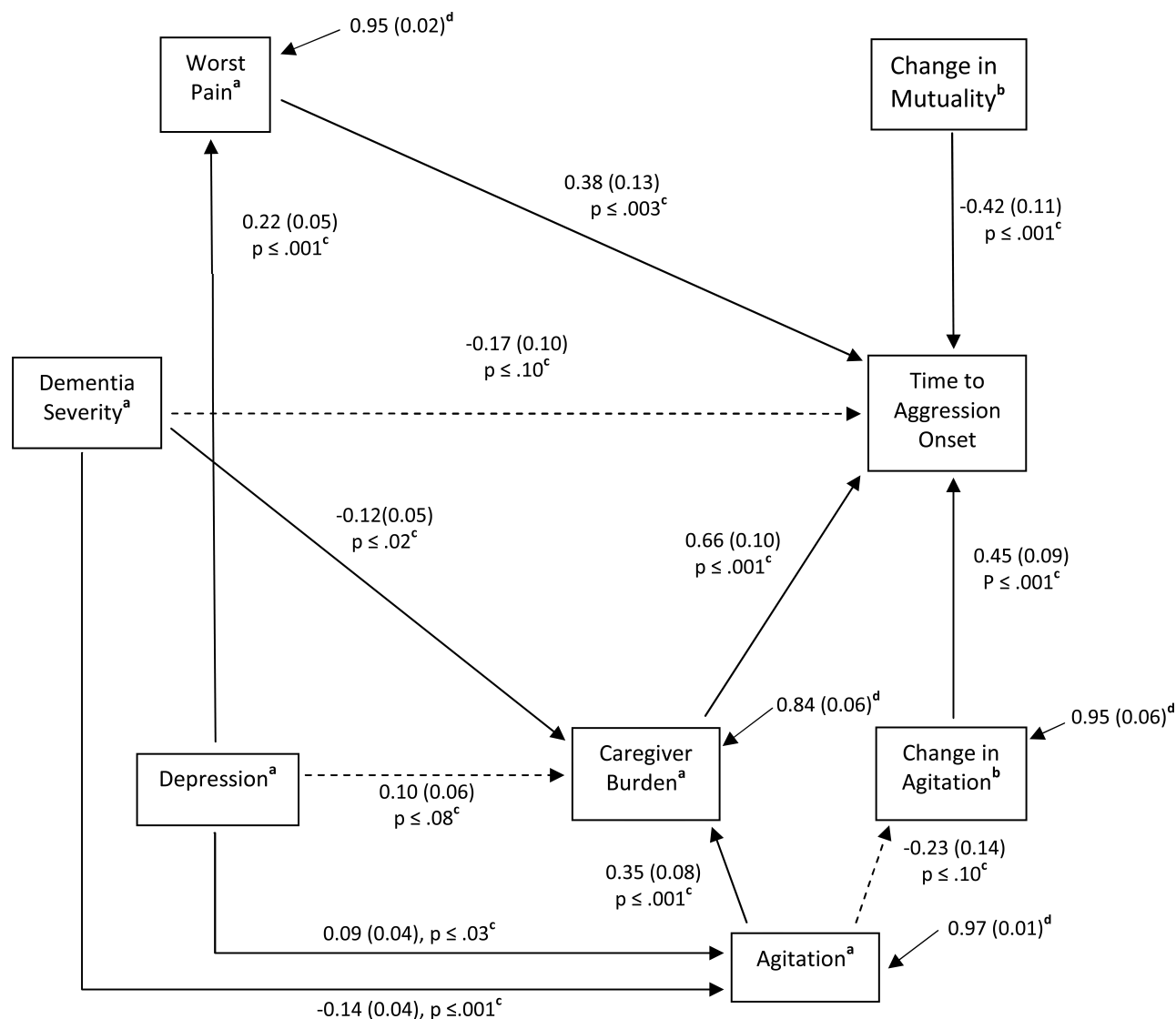


Figure 1. Final model predicting time to onset of aggression.

^aBaseline measure.

^bEstimated 12-month Rate of Change.

^cStandardized B(SE), p-value.

^dStandardized Residual Variance.

pain, depression, caregiver burden, and a declining quality of relationship between the patient and caregiver) all share the characteristic of mutability. Effective interventions are available to address each of these factors, and our findings suggest that clinical resources should be focused on these important issues to prevent the potentially dangerous and costly development of physical aggression in this vulnerable population.

It appears that early intervention and identification of patients exhibiting nonaggressive, physical agitation is essential to prevent progression to aggression. Conceptual models focused on unmet needs have been influential in guiding researchers

and clinicians to investigate these needs as causes of agitation and distress. However, as helpful as those models have been, they have not been able to guide us in predicting the causes of aggression (Kovach, Noonan, Schlidt, & Wells, 2005; Whall & Kolanowski, 2004). Given our findings and the findings of others of significant associations between agitation and the development of aggression (Aarsland et al., 1996; Gormley et al., 1998), such models might be revised to state that reducing agitation may be an important step in preventing aggression. Further, the association between our baseline measures of depression and nonaggressive physical agitation is consistent with recent work

by Volicer, Frijters, and Van der Steen (2012) who linked depressive symptoms with agitation among Dutch nursing home residents over time. Our work supports and extends their findings by suggesting links through which depression may affect the time to aggression onset.

The associations with onset of aggression that we identified for caregiver burden and change in the patient-caregiver relationship are consistent with the link between patient resistiveness, caregiving approach, and aggression proposed by Volicer and Hurley (2003). Caregiver burden and quality of the patient-caregiver relationship are potentially modifiable factors and, hence, interventions that focus on supporting caregivers and their ability to maintain quality relationships with their loved one with dementia, such as REACH VA, can be implemented (Nichols, Martindale-Adams, Burns, Graney, & Zuber, 2011). In conjunction, programs are available to reduce wandering, which is one form of non-aggressive physical agitation (Robinson et al., 2007) and may consequently reduce strain between the caregiver and the patient. Finally, there is a significant body of literature on the importance of careful pain assessment and treatment in persons with dementia (Feldt, Warne, & Ryden, 1998; Zwakhalen, Koopmans, Geels, Berger, & Hamers, 2009).

In sum, this is the first longitudinal study to examine direct and indirect relationships between psychosocial factors and aggression. We identified potentially mutable factors that were associated with development of aggression. Our findings suggest that careful assessment of these psychosocial factors should be a routine part of clinical care for persons with dementia, followed by effective treatment and follow-up of such conditions when identified. Such interventions may reduce risk of harm to persons with dementia and their caregivers (Kunik et al., 2010a).

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