Published in final edited form as:

Alzheimer Dis Assoc Disord. 2011 ; 25(2): 109–115. doi:10.1097/WAD.0b013e3181f8520a.

Undiagnosed Illness and Neuropsychiatric Behaviors In Community-residing Older Adults with Dementia¹

Nancy Hodgson, Ph.D., RN², Laura N. Gitlin, Ph.D.³, Laraine Winter, Ph.D.⁴, and Kathleen Czekanski, Ph.D., RN⁵

Laura N. Gitlin: laura.gitlin@jefferson.edu; Laraine Winter: laraine.winter@jefferson.edu

³ Director, Jefferson Center for Applied Research on Aging and Health, Thomas Jefferson University, 130 S. 9th Street, Suite 513, Philadelphia, PA, 19130

⁴ Assistant Director, Jefferson Center for Applied Research on Aging and Health, Thomas Jefferson University, 130 S. 9th Street, Suite 500, Philadelphia, PA, 19130; voice - 215-503-4715; fax- 215-923-2475

⁵ Nurse Interventionist, Jefferson Center for Applied Research on Aging and Health, Thomas Jefferson University, 130 S. 9th Street, Suite 500, Philadelphia, PA, 19130; voice - 215-951-1322

Abstract

The aim of this retrospective analysis was to examine prevalence of undiagnosed acute illness and characteristics including neuropsychiatric symptoms associated with illness in community-residing older adults with Alzheimer's disease or related disorders. Subjects included 265 community-residing older adults with dementia who participated in one of two interventions being tested in randomized clinical trials. Measures included a brief nursing assessment and lab evaluations including complete blood count (CBC), blood chemistry (Chem 7), and thyroid function tests of serum samples and culture and sensitivity tests of urine samples. Undiagnosed illness was identified according to currently published criteria. Neuropsychiatric behaviors were assessed using 21 behaviors derived from standard measures. Thirty-six percent (N= 96) of patients had clinical findings indicative of undetected illness. Conditions most prevalent were bacteriuria (15%), followed by hyperglycemia (6%) and anemia (5%). The behavior most often demonstrated among those with detected illness was resisting or refusing care (66% versus 47% for those without detected illness). Individuals with detected illness had significantly lower functional status scores (3.8 vs. 4.4, $t(275) = 7.01$, $p = .01$), lower cognitive status scores (10.5 vs. 14.4, $t(275) = 12.1$, $p < .01$) and were more likely to be prescribed psychotropic medications for behavior (41% vs. 26%, $\chi^2 = 3.67$, $p < .05$) than those without illness. Findings suggest that challenges of diagnosing acute illness with atypical presentation must be addressed to promote quality of care and the specialized needs for this vulnerable population.

Keywords

Comorbidity; frailty; home care

¹Funded by the National Institute on Aging and National Institute on Nursing Research Grant #R01 AG22254 and PA Department of Health SAP #100027298

²Corresponding Author; Research Scientist, Jefferson Center for Applied Research on Aging and Health, Thomas Jefferson University, 130 S. 9th Street, Suite 500, Philadelphia, PA, 19130; voice -215-955-2163; fax- 215-923-2475; nancy.hodgson@jefferson.edu.

Clinical Trial Registrations: #NCT00259480; NCT00259454

INTRODUCTION

Previous research suggests that individuals with dementia may suffer from undiagnosed medical illnesses disproportionately more than those without cognitive impairment^{1–3}. Prevalence rates range from 50% to 66%.;however, rates have been mostly reported for inpatient or institutionalized samples^{4,5} versus for community-dwelling individuals with dementia where the majority live. Undiagnosed but treatable medical conditions such as urinary tract infection or anemia may contribute to neuropsychiatric behaviors and poor life quality. Common neuropsychiatric behaviors such as resistance to care, repetitive vocalizations or aggressiveness represent one of the most challenging, emotionally burdensome, and costly aspects of caring for individuals with dementia. Thus, identifying prevalence rates and determining the role of undiagnosed medical illnesses in behavioral symptom presentation is important to derive the best clinical management of community-residing individuals with dementia.

Identifying underlying illness poses a significant clinical challenge as individuals with dementia may not be able to adequately communicate their symptoms, particularly at the moderate to severe disease stage⁷. For example, older adults with dementia often cannot reliably report classic symptoms of urinary tract infections (UTI), such as dysuria, itching, or urinary burning or frequency^{8,9}. Moreover, older adults may have atypical or asymptomatic presentations of acute illness with insidious presentation¹⁰. Left untreated, these illnesses can lead to delirium further worsening behavioral symptomatology¹¹.

Anecdotal reports and clinical case studies provide preliminary evidence that individuals with dementia may display an increase in neuropsychiatric symptoms before the onset of acute illness such as dehydration, hyperglycemia or infection¹². The electrolyte disturbances associated with dehydration may result in challenging behaviors such as restlessness, delusions, or agitation¹³. Specific symptoms associated with hyperglycemia include mood irritability, and mental status changes¹⁴. Behaviors of physical agitation have also been found to be prodromal to the development of infection^{15–17}. Other incipient illnesses such as thyroid disorders or anemia can result in behavior changes that manifest in the form of irritable or erratic mood, lethargy, and restlessness^{18–21}.

Thus, although incipient illness is recognized as a potential contributor to behaviors, this relationship needs further substantiation. The purpose of this exploratory study was to evaluate the relationship of undiagnosed illness and neuropsychiatric behaviors in community residing older adults with dementia. Specifically we sought to: 1) describe the prevalence of undiagnosed medical conditions; and 2) identify characteristics associated with the presence of undiagnosed medical illness in a community residing population of older adults with dementia. To examine prevalence, we used data collected in two distinct randomized trials as part of the interventions being tested. One trial, Advancing Caregiver Training (Project ACT) collected data in 2005–2008 from 136 informal caregivers and dementia patients assigned to an intervention designed to target the most pressing neuropsychiatric symptoms causing caregiver distress and 22 control group subjects who completed the original trial and then were assigned to a supplemental study arm to receive an intervention for a total of 158²². Second, we used data collected in 2006–2009 from 107 caregivers and dementia patients randomly assigned to a home-based intervention designed to address functional and behavioral challenges called Care of Persons with Dementia in their Environment (COPE²³). In both studies, one component of the interventions involved a home visit from an advance practice nurse who provided caregiver education about potential medical problems contributing to behavioral occurrences (e.g., dehydration, constipation, pain), and performed a brief nursing assessment. To uncover possible undiagnosed illness, serum and urine samples were collected. Laboratory evaluations included Chem 7 and

thyroid testing of serum samples, and culture and sensitivity of urine samples. The nurse contacted caregivers by telephone to review laboratory results and mailed two copies (for caregiver and physician). For positive results, the nurse coordinated physician contact if needed.

METHODS

Study Sample and Procedures

Projects ACT and COPE have been described elsewhere^{22,23}. Briefly, in both trials, family caregivers and their family members with dementia living in a five county area of the Philadelphia region were enrolled. Eligibility criteria for study participation for both trials were similar and included the following: Caregivers were English speaking, over the age of 21, caring at home for more than 3 hours a day for a person with either a physician diagnosis of dementia or Mini Mental State Examination²⁴(MMSE) score less than 24. Individuals with dementia were excluded if they had schizophrenia, bipolar disorder, or dementia secondary to head trauma, or had an MMSE score = 0 and were also bed-bound or nonresponsive. For the ACT trial, caregivers had to report the occurrence of one or more behavioral symptoms and upset level >5 (out of 10); whereas for the COPE trial, caregivers had to report occurrence of one or more behavioral symptoms or any difficulty in performing caregiving duties. For both studies, caregivers who contacted the research team were initially screened by telephone and then interviewed at home, following signage of an IRB approved informed consent and proxy consent forms. Assent from the person with dementia was obtained at the administration of each assessment. Dyads were randomized to intervention or a control group following the baseline interview. The nurse visit was one component of the in-home caregiver supportive and skills training programs tested in the trials. The data derived from that visit in both trials is the focus of the current study. Additionally, data derived from the baseline interview conducted by a trained interviewer prior to randomization was examined for those assigned to the intervention groups..

Nurse Assessment

The nurse protocol was the same for both trials. To uncover possible episodes of acute illness, a trained nurse researcher completed a brief medical history of the person with dementia from the caregiver. The nurse also conducted a physical examination to observe for signs of dehydration (skin elasticity, capillary refill, mucous membranes, self report of urine output) and obtained serum and urine samples for laboratory analysis from the person with dementia. The laboratory evaluations included complete blood count (CBC), Chem 7 blood chemistry, and thyroid function tests of serum samples, and culture and sensitivity tests of urine samples that indicated the presence of nitrites/leukocytes/blood after dipstick.

Prescription medications were also reviewed to evaluate for possible polypharmacy and for use of medications with central anticholinergic activities and psychotropic medications, such as antidepressants, anxiolytics and antipsychotics. The presence of new, previously undiagnosed illness was then determined based on currently published guidelines^{25–27}(Table 1). Acute illnesses that were identified included urinary tract infection, hyper/hyponatremia, hyper/hypoglycemia, hyper/hypokalemia, dehydration and anemia. Following the nurse visit, the nurse contacted each family caregiver by telephone within two days to inform him/her of laboratory results (whether positive or negative). If positive, the nurse informed the caregiver to contact the doctor immediately and coordinated contact if requested by the caregiver. She then followed up again by telephone with the caregiver to obtain an update as to whether physician consultation was sought and if so, the course of treatment prescribed.

Measures

In both studies, background characteristics of the person with dementia and caregiver included age, gender, marital status (married, unmarried), self-identified race, and mental status (MMSE). In order to assess functional status, caregivers were asked to report the level of assistance required for the person with dementia to perform basic activities of daily living (ADL) using the Caregiver Assessment of Function and Upset (CAFU) scale²⁸. The CAFU provides a reliable and valid approach to evaluating traditional areas of physical function as well as which areas of functional dependence are upsetting to caregivers. The CAFU consists of six ADL items related to eating, grooming, bathing, dressing upper body, dressing lower body, toileting, transferring to bed/chair/wheelchair. Each item is rated with a score from 1 to 7 (1=complete assistance, 2=maximal assistance, 3=moderate assistance, 4=minimal assistance, 5=supervision, 6=modified independence, and 7=complete independence) (Chronbach's $\alpha = .73$).²⁸

Neuropsychiatric behaviors—To examine neuropsychiatric behaviors, we used 21 behavioral items of which 16 were derived from the Agitated Behavior in Dementia (ABID) Scale²⁹. The ABID has been previously shown to be psychometrically sound and corresponding to objective reports of commonly presenting symptoms (e.g. verbal aggressiveness, physical aggressiveness, screaming/crying out, behaviors harmful to self, roaming, destroying property, resisting/refusing care, arguing/irritability, socially inappropriate behavior, inappropriate sexual behavior, easily agitated/upset, restlessness, fearful/anxious, getting up at night, distressing beliefs, seeing/hearing distressing people/things). Validity of the ABID has been confirmed by correlations with related measures and lack of correlation with unrelated constructs. Overall scale reliability is acceptable ($\alpha = .78$ for our sample and test-retest reliability of 0.60 to 0.73). We also included 2 items (repetitive questioning, hiding/hoarding) from the Revised Memory and Behavior Problem Checklist (RMBPC)³⁰, and 3 items (wandering, incontinence, shadowing) from our previous research showing these behaviors as common and distressful³¹.

Data Analysis

Descriptive statistics were used to describe the prevalence of undiagnosed illness with each trial and across both samples. Chi square or t tests were used to compare the characteristics of participants with undiagnosed illness to those without undiagnosed illness using the total combined sample. Significant factors from the univariate analysis were tested in multivariable models to assess the impact of the combined predictors. Next, the association between presence of specific undiagnosed illnesses and each of the 21 neuropsychiatric behaviors was assessed using Phi coefficient correlations using the combined sample. Data analysis was performed using STATA software, version 10 for Windows (StataCorp, College Station, Texas) with a significance level set at .05.

RESULTS

Persons with dementia in the combined datasets ranged in age from 58 to 99 with an average age of 82.7 years (SD 8.2). Most were female (59%) and white (70%), with average mental status scores indicating a low to moderate cognitive functioning (MMSE mean = 13, SD = 8). Caregivers reported that individuals with dementia required a moderate level of assistance with ADL's (Mean = 7.41, $\pm$ SD = 1.8) and demonstrated an average of 10 (SD = 4) out of 21 neuropsychiatric behaviors. Most persons with dementia were taking one or more medications with 37% on depression medications, 33% on medications for behaviors, 40% on pain medications, and 72% on memory enhancement dementia medications. Caregivers were also primarily female (83%) and White (71%), and were on average 65 years of age (Table 2). The COPE and ACT participants differed significantly with regards to three

demographic characteristics. Individuals with dementia in the COPE sample were predominantly female (77%), whereas the gender of the ACT sample subjects was more evenly distributed ($\chi^2 = 17.84$; $p < .01$). Caregivers in the COPE sample were largely non-spouses (69%), whereas the marital status of caregivers in the ACT sample were more evenly distributed ($\chi^2 = 7.46$; $p = .01$). Lastly, caregivers in the ACT sample had significantly higher levels of education than caregivers in the COPE sample (62% > high school education for ACT vs. 38% > high school education for COPE; $\chi^2 = 19.38$; $p < .01$).

Prevalence of Medical Conditions

Of the 265 participants in the combined sample, blood samples were obtained from 226 (85%) subjects (6 subjects refused and 32 subjects were unable to provide a sample) and urine samples were obtained from 243 (92%) subjects (6 subjects refused and 22 were unable to provide a sample). Undiagnosed acute illnesses occurred in 56 individuals with dementia in Project ACT, 40 individuals in COPE and 96 (36%) for the combined sample (Table 1) for which the nurse recommended that the caregiver seek physician follow-up. For the combined sample, the most prevalent conditions were bacteriuria (15%), followed by anemia (6%) and hyperglycemia (5%).

Treatment of Conditions

Of the 96 individuals with detected illness, 92 (95%) caregivers followed up with a doctor; one caregiver dropped out of the trial and was lost to follow-up and three caregivers chose not to follow-up with the subjects' physicians. Of 92 with physician follow-up, one doctor did not treat (subject had asymptomatic bacteriuria), one subject was hospitalized due to lab results and all others were treated on an outpatient basis.

Characteristics Associated with Undiagnosed Illness

Characteristics associated with the presence of undiagnosed undetected illness are reported in Table 3. No large or statistically significant differences in subject demographic and background characteristics were present between those with detected illness ($N=96$) and those without detected illness ($N=179$). However, individuals with detected illness had significantly lower functional status scores (3.8 vs. 4.4, $t(275) = 7.01$, $p = .01$), lower MMSE scores (10.5 vs. 14.4, $t(275) = 12.1$, $p < .01$) and were more likely to be prescribed psychotropic medications for behavior (41% vs. 26%, $\chi^2 = 3.67$, $p < .05$) than those without illness.

Neuropsychiatric Symptoms and Specific Illnesses

The behavior most often demonstrated among those with detected illness was resisting or refusing care (66%), compared to 47% of those without any detected illness ($\chi^2 = 5.44$, $p = .02$). Table 4 shows significant Phi correlation analysis between specific detected illnesses including bacteriuria, hyperglycemia, anemia and metabolic disturbances (hyponatremia, hypokalemia, thyroid disorders), and various neuropsychiatric symptoms. The data reveal statistically significant but small correlations between bacteriuria and both incontinence ($p < .02$) and agitation ($p = .02$). Statistically significant correlations were also found between hyperglycemia and both agitation and repetitive vocalizations ($p < .05$). Anemia was significantly associated with crying out behavior ($p = .03$). Metabolic disturbances such as hyponatremia, hypokalemia and thyroid disorders were significantly associated with the presence of delusions, hallucinations and agitation (all $p < .05$).

DISCUSSION

This exploratory study describes the prevalence and characteristics associated with undiagnosed illness in community residing individuals with dementia. Our findings confirm previous estimates of high prevalence of undetected but modifiable illnesses in individuals with dementia¹⁰, with 36% of participants exhibiting clinically significant signs of previously unidentified illness. Bacteriuria, hyperglycemia and anemia were the most prevalent illnesses in the sample, accounting for 25% of the illnesses across both samples.

Specifically, bacteriuria accounted for 15% of the undiagnosed illness in our combined sample which is consistent with previous estimates of urinary tract infection rates in individuals with dementia¹⁶. However, distinguishing asymptomatic bacteriuria from urinary tract infection (UTI) in older adults with dementia remains a diagnostic challenge^{8,9}. Multiple illnesses may present with symptoms similar to UTI, and individuals with dementia may not be able to report symptoms. Thus, further work is needed to distinguish these two conditions³².

Our finding of a prevalence rate of anemia of 6% is slightly higher than previous investigations of community-based samples³³. Beghe Wilson & Ershler observed rates of undiagnosed anemia of 4.4% in men and 3.9 % of women in a sample of community residing elders³⁴. The shared risk factors for anemia and dementia may account for the higher rates found in our sample³⁵. Anemia prevalence rates in frail elders is 4 times the national estimates for non-frail older adults (39.6% in men and 37.9% in women)³³. In samples comparing older adults with and without dementia, older adults with dementia were found to be at twofold risk for anemia primarily attributed to folate deficiencies and increased homocysteine levels³⁵.

Hyperglycemia accounted for 5% of undiagnosed illness in the sample. Recent research has begun to focus on the higher rates of hyperglycemia among persons with dementia, and suggest that these rates are a result of psychotropic medication use^{36–37}. The heightened interest in the effects of psychotropic drugs on glucose metabolism reflects the current concern about atypical antipsychotics as risk factors for diabetes, hyperlipidemia, and obesity. Undiagnosed hyperglycemia is associated with significantly higher mortality rates and poor clinical outcomes in individuals both with and without a history of dementia^{38–39}. Reports of severe hyperglycemia with ketoacidosis shortly after initiating treatment with atypical antipsychotics, even in the absence of weight gain, have fostered studies of possible effects of these agents on insulin secretion. In our sample, individuals with hyperglycemia were prescribed antipsychotic medications at slightly higher rates than in those without glucose imbalances (52% vs. 48%); however these relationships were not significant.

The rates of other underlying metabolic disorders were infrequent in our sample and are in line with reports from previous studies with similar community samples of older adults with dementia⁵. However, metabolic disorders such as hypothyroidism—even when occult or subclinical—can cause subtle or frank changes in energy, mood, anxiety level, or cognition and may explain the neuropsychiatric symptoms present in this subgroup⁴⁰.

Regarding associations between behavior symptoms and medical conditions, the data also suggest that certain neuropsychiatric behaviors in older adults with dementia may signal incipient acute illness. It seems plausible that the discomfort resulting from undetected conditions could lead to refusal of care or agitation. In this study, refusing care was more predictive of illness than other nonspecific symptoms, and agitation was associated with illnesses such as bacteriuria and metabolic disorders. The findings suggest that health care providers should pay particular attention to individuals with these symptoms⁴¹.

Dementia complicates the medical management of older adults residing in the community. Given that underutilization of medical care has been documented among community-residing elders with dementia^{1,3}, the high prevalence of undiagnosed illness may not be surprising. Despite higher rates of comorbid conditions, dementia subjects tend to report fewer symptoms and complaints during visits with their primary care physicians⁴². Although geriatric practitioners may be skilled at identifying behavior such as agitation, that accompany acute illnesses,¹⁵ family caregivers may not recognize this association. However, it is important to note that clinicians often misinterpret behaviors as signaling a need for increased psychotropic medication,²¹ or caregiver training rather than determining whether there is an undetected medical condition¹⁸. Thus, many older adults may be quietly suffering from unrecognized illnesses leading to under treatment, wrong treatments or unmet medical needs.

Individuals with an undetected illness had lower functional ability and lower MMSE scores when compared to those without illness. The worsening of cognitive and functional status observed in our sample with undiagnosed illness may be an indicator or potential risk factor for an underlying illness signaling the need for additional assessment to rule out an underlying illness.

Identifying unmet health needs is an important part of community-based health care for individuals with dementia. Since these medical concerns typically reside in the domain of primary care, these providers must be particularly vigilant in detecting underlying medical illnesses. Studies of older adults with acute illness have shown that presenting symptoms and signs can be atypical and nonspecific,⁴² which may hinder timely diagnosis and treatment. Careful physical assessment is often the most useful part of the medical evaluation and extensive, and expensive, diagnostic evaluations may not be required. The illnesses identified in this sample were derived from simple, low cost medical testing which can be performed in home or primary care; thus, specialized medical testing may not be necessary for the on-going medical management of individuals with dementia who manifest behavioral symptoms and who show functional decline.

Several limitations of these findings should be noted. The study is cross-sectional and thus we can not confirm causality. Also, participants may not be fully representative of the community-residing dementia population and may have biased the prevalence estimates. However, given that similar prevalence rates were detected for two distinct trial samples suggests that our findings may be generalizable at least to those community-residing patients who experience functional or behavioral symptoms, an eligibility requirement for both trials. Nevertheless, without a comparator group of non-demented participants, we are unable to determine the extent to which dementia confounds the diagnosis of underlying medical problems. Another limitation is the reliance on caregiver report of behavioral occurrences. Proxy caregiver reports of behavior including biases that overestimate or underestimate actual behaviors may result from the timing of the assessment or other caregiver characteristics⁴³. However, we used psychometrically valid instruments, the ABID and RMBPC, and use of collateral information remains the primary data source of behaviors in both research and clinical evaluations. Sample size limitations prevented our ability to control for potential confounders. For example, we were unable to control for stage of dementia as an important factor influencing neuropsychiatric symptoms observed. An additional limitation is that although subjects in this study all had a primary care doctor, it is unclear how often they visited their physicians, whether blood and urine samples were routinely evaluated and the time between physician visit, study participation, and detection of illness. Determination of dehydration was based on direct observation of physical symptoms including skin turgor and elasticity, which can be poor measures of hydration status in individuals with dementia⁴⁴. Thus, it is difficult to discern whether some subjects

had more frequent contact than others with their physicians and how this effects the prevalence rates we report here. In addition, laboratory analyses did not include assessment of other commonly missed diagnoses in this population including renal or liver dysfunction, pulmonary disease, or possible coagulopathies.

Moreover, our results cannot unravel the underlying mechanism explaining the high rates of illness in the sample. Speculatively, the effects may be partially attributed to concomitant use of psychotropic medications. Because we did not collect data on the reasons for prescribing anticholinergics or antipsychotic, judgments cannot be made about the appropriateness of these medications in our sample⁴⁵. Lastly, our study design did not permit us to determine if neuropsychiatric symptoms resolved following medical treatment alone.

Nevertheless, this study is the first to our knowledge to evaluate prevalence of treatable illness and their relationship to behaviors. While the data are preliminary, they shed light on the complexity of caring for adults with dementia and suggest that we need to carefully re-examine their medical management. The overall illness burden in our sample may explain the prevalence rates of undiagnosed illness and the difficulty facing clinicians in recognizing new problems. Unfortunately, current clinical guidelines for the primary care of older adults with dementia offer physicians little in the way of direction⁴⁶. Closer scrutiny of the prescribing patterns for persons with dementia is needed to assess for ways to reduce excess disability and morbidity. Future investigation is warranted to determine whether proactive clinical evaluation of behavioral symptoms can prevent or postpone development of undetected illness. Early detection of acute illness may result in treatment that improves behavioral symptoms and other outcomes such as worsening of cognitive and physical functioning and resulting caregiver burden. Prospective controlled trials are especially needed to determine if earlier diagnoses and treatment of underlying illnesses may alter the progression of disease. For example, intervention studies are needed to establish whether the correction of anemia affects cognitive improvement or forestalls hospitalization or institutionalization. As preventative primary care assessment has been shown to reduce occurrence of untoward events in nursing home residents with dementia^{47–49}, this approach with community-based persons with dementia, where the majority live, may have similar positive outcomes.

Acknowledgments

We gratefully thank Walter Hauck, PhD, Ruth Mooney, PhD, RN, the Project ACT and COPE research staff and study participants for their time and responses.

References

1. Capi E, Silverstein NM, Porell F. Physician outpatient contacts and hospitalizations among cognitively impaired elderly. *Alz Dement*. 2009; 5(1):30–42.
2. Maslow K. Dementia and serious coexisting medical conditions: a double whammy. *Nurs Clin North Am*. 2004 Sep; 39(3):561–79. [PubMed: 15331302]
3. Walsh EG, Wu B, Mitchell JB, et al. Cognitive function and acute care utilization. *Gerontol B Psychol Sci Soc Sci*. 2003; 58(1):S38–49.
4. Larson EB, Reifler BV, Sumi SM, et al. Diagnostic evaluation of 200 elderly outpatients with suspected dementia. *J Gerontol*. 1985; 40(5):536–43. [PubMed: 4031401]
5. Doraiswamy PM, Leon J, Cummings JL, et al. Prevalence and impact of medical comorbidity in Alzheimer's disease. *J Gerontol A Biol Sci Med Sci*. 2002; 57(3):M173–7. [PubMed: 11867654]
6. Marengoni A, Rizzuto D, Wang HX, et al. Patterns of chronic multimorbidity in the elderly population. *J Am Geriatric Soc*. 2009 Feb; 57(2):225–30.

7. McCloskey R. Caring for patients with dementia in an acute care environment. *Geriatr Nurs*. 2004; 25(3):139–44. [PubMed: 15197372]
8. Walker S, McGeer A, Simor AE, et al. Why are antibiotics prescribed for asymptomatic bacteriuria in institutionalized elderly people? *CMAJ*. 2000; 163:273–277. [PubMed: 10951723]
9. Miller J. To treat or not to treat: managing bacteriuria in elderly people. *CMAJ*. 2001; 164:619–620. [PubMed: 11258205]
10. Lopponen MK, Isoaho RE, Raiha IJ, et al. Undiagnosed diseases in patients with dementia—a potential target group for intervention. *Dement Geriatr Cogn Disord*. 2004; 18(3–4):321–9. [PubMed: 15305110]
11. Woods DL, Menten JC. Agitated behavior as a prodromal symptom of physical illness: a case of influenza. *Current awareness in geriatric psychiatry*. *International J Geriatr Psych*. 2007; 22:9, 937.
12. Amella EJ. Presentation of illness in older adults. If you think you know what you're looking for, think again. *AORN J*. 2006; 83(2):372–4. 377–82, 385–9. [PubMed: 16544857]
13. Leger JM, Moulias R, Robert P, et al. Agitation and aggressiveness among the elderly population living in nursing or retirement homes in France. *Int Psychogeriatr*. 2002; 14(4):405–16. [PubMed: 12670061]
14. Arinzon Z, Fidelman Z, Berner YN, et al. Infection-related hypoglycemia in institutionalized demented patients: a comparative study of diabetic and nondiabetic patients. *Arch Gerontol Geriatr*. 2007; 45(2):191–200. [PubMed: 17169447]
15. Alessi C, Harker J. A prospective study of acute illness in the nursing home. *Aging Clin Exp Res*. 1998; 10:479–489.
16. Boockvar KS, Lachs MS. Predictive value of nonspecific symptoms for acute illness in nursing home residents. *J Am Geriatr Soc*. 2003; 51:1111–1115. [PubMed: 12890074]
17. Nicolle LE. Urinary tract infections in long-term care facilities. *Infect Control Hosp Epidemiol*. 2001; 22:167–175. [PubMed: 11310697]
17. Stamm WE, Raz R. Factors contributing to susceptibility of postmenopausal women to recurrent urinary tract infections. *Clin Infect Dis*. 1999; 28:723–726. [PubMed: 10825026]
18. Davis JD, Tremont G. Neuropsychiatric aspects of hypothyroidism and treatment reversibility. *Minerva Endocrinol*. 2007; 32(1):49–65. [PubMed: 17353866]
19. de Jong FJ, Masaki K, Chen H, et al. Thyroid function, the risk of dementia and neuropathologic changes: The Honolulu-Asia Aging Study. *Neurobiol Aging*. 2009; 30(4):600–6. [PubMed: 17870208]
20. Cardenas-Ibarra L, Solano-Velazquez JA, Salinas-Martinez R, et al. Cross-sectional observations of thyroid function in geriatric Mexican outpatients with and without dementia. *Arch Gerontol Geriatr*. 2008 Mar-Apr; 46(2):173–80. [PubMed: 17512618]
21. Johnson JC, Jayadevappa R, Baccash PD, et al. Nonspecific presentation of pneumonia in hospitalized older people: Age effect or dementia? *J Am Geriatr Soc*. 2000; 48:1316–1320. [PubMed: 11037021]
22. Gitlin LN, Winter L, Dennis M, et al. A non-pharmacological intervention to manage behavior and psychological symptoms of dementia and reduce caregiver distress: Design and methods of project ACT. *Clin Int Aging*. 2007; 2:695–703.
23. Gitlin LN, Winter L, Dennis M, et al. Project Enhancing Daily Function and Quality of Life of Patients with Dementia and the Well-being of Caregivers: A Nonpharmacologic Randomized Trial. *JAMA*. 2010 in press.
24. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975; 12(3):189–98. [PubMed: 1202204]
25. World Health Organization. The Treatment of Diarrhea: A Manual for Physicians and Other Senior Health Workers. Geneva, Switzerland: World Health Organization; 1995. WHO/CDD/SER/80.2 Rev. 3
26. Surks MI, Chopra IJ, Mariash CN, Nicoloff JT, Solomon DH. American Thyroid Association guidelines for use of laboratory tests in thyroid disorders. *JAMA*. 1990; 263:1529–1532. [PubMed: 2308185]

27. Boockvar KS, Lachs MS. Development of definitions for acute illness in nursing home residents based on chart-recorded physical exam findings. *J Am Med Direct Assoc.* 2001; 2:279–284.
28. Gitlin LN, Roth DL, Burgio LD, et al. Appraisals of Functional Dependence in Individuals With Dementia and Associated Caregiver Upset: Psychometric Properties of a New Scale and Response Patterns by Caregiver and Care Recipient Characteristics. *J Aging Health.* 2005 Apr; 17(2):148–71. [PubMed: 15750049]
29. Logsdon RG, Teri L, Weiner MF, et al. Assessment of agitation in Alzheimer's disease: The agitated behavior in dementia scale. *J Am Geriatr Soc.* 1999; 47:1354–1358. [PubMed: 10573447]
30. Teri L, Truax P, Logsdon R, et al. Assessment of behavioral problems in dementia: The Revised Memory and Behavior Problems Checklist (RMBPC). *Psychol Aging.* 1992; 7:622–631. [PubMed: 1466831]
31. Gitlin LN, Winter L, Corcoran M, et al. Effects of the home environmental skill-building program on the caregiver-care recipient dyad: 6-month outcomes from the Philadelphia REACH Initiative. *Gerontologist.* 2003; 43(4):532–546. [PubMed: 12937332]
32. Juthani-Mehta M, Quagliarello V, Perrelli E, Towle V, Van Ness PH, Tinetti M. Clinical features to identify urinary tract infection in nursing home residents: a cohort study. *J Am Geriatric Soc.* 2009; 57(6):963–70.
33. Argento V, Roylance J, Skudlarska B, et al. Anemia prevalence in a home visit geriatric population. *J Am Med Dir Assoc.* 2008; 9(6):422–426. [PubMed: 18585644]
34. Beghe C, Wilson A, Ershler WB. Prevalence and outcomes of anemia in geriatrics: a systematic review of the literature. *Am J Med.* 2004 Apr 5; 116(Suppl 7A):3S–10S. [PubMed: 15050882]
35. Beard CM, Kokmen E, O'Brien PC, et al. Risk of Alzheimer's disease among elderly patients with anemia: population-based investigations in Olmsted County, Minnesota. *Ann Epidemiol.* 1997; 7(3):219–24. [PubMed: 9141646]
36. Lipscombe LL, Levesque L, Grunier A, et al. Antipsychotic drugs and hyperglycemia in older patients with diabetes. *Arch Intern Med.* 2009; 27;169(14):1282–9.
37. Zheng L, Mack WJ, Dagerman KS, et al. Metabolic changes associated with second-generation antipsychotic use in Alzheimer's disease patients: the CATIE-AD study. *Am J Psychiatry.* 2009; 166(5):583–90. [PubMed: 19369318]
38. Asadollahi K, Hastings IM, Beeching NJ, et al. Laboratory risk factors for hospital mortality in acutely admitted patients. *QJM.* 2007; 100(8):501–507. [PubMed: 17609227]
39. Kosiborod M, Inzucchi SE, Spertus JA, et al. Elevated admission glucose and mortality in elderly patients hospitalized with heart failure. *Circulation.* 2009; 119(14):1899–1907. [PubMed: 19332465]
40. Bembien DA, Winn P, Hamm RM, et al. Thyroid disease in the elderly. Part 1. Prevalence of undiagnosed hypothyroidism. *Fam Pract.* 1994 Jun; 38(6):577–82.
41. Emmett KR. Nonspecific and atypical presentation of disease in the older patient. *Geriatrics.* 1998; 53:58–60.
42. Boustani M, Schubert C, Sennour Y. The challenge of supporting care for dementia in primary care. *Clin Interv Aging.* 2007; 2(4):631–6. [PubMed: 18225464]
43. Woods DL, Bushnell B, Kim H, Geschwind D, Cummings J. Apolipoprotein epsilon4 status is associated with behavioral symptoms in nursing home residents with dementia. *Int Psychogeriatr.* 2009 Aug; 21(4):722–8. [PubMed: 19470200]
44. Menten JC, Wang J. Measuring Risk for Dehydration in Nursing Home Residents. *Res Gerontol Nurs.* 2010 May; 31:1–9. [PubMed: 20509595]
45. Campbell N, Boustani M, Limbil T, et al. The cognitive impact of anticholinergics: A clinical review. *Clin Interv Aging.* 2009; 4(1):225–33. [PubMed: 19554093]
46. Callahan CM, Boustani M, Sachs GA, et al. Integrated care for older adults with cognitive impairment. *Curr Alzheimer Res.* 2009; 6(4):368–374. [PubMed: 19689236]
47. Ackermann RJ, Kemle KA. The effect of a physician assistant on the hospitalization of nursing home residents. *J Am Geriatr Soc.* 1998; 46:610–614. [PubMed: 9588375]
48. Kane RL, Keckhafer G, Flood S, et al. The effect of Evercare on hospital use. *J Am Geriatr Soc.* 2003; 51(10):1427–34. [PubMed: 14511163]

49. Kane RL, Flood S, Bershadsky B, et al. Effect of an innovative Medicare managed care program on the quality of care for nursing home residents. *Gerontologist*. 2004; 44(1):95–103. [PubMed: 14978325]

Table 1

Frequencies of Undiagnosed Undetected Illness in Study Sample

Diagnosis	Definition	ACT sample ^a (N=158)	COPE sample ^b (N=107)	Total Study Sample (N=265)
Bacteriuria	Urinalysis results positive for nitrates, blood, or leukocytes, urine culture and sensitivity tests positive for bacteriuria	22 (14%)	15 (15%)	37 (14%)
Anemia	Hemoglobin level less than 11.7 g/dl and hematocrit <35%	7 (4%)	9 (7%)	16 (6%)
Hyperglycemia	Serum glucose above 200.0 mg/dl	10(6%)	5 (5%)	15 (5%)
Dehydration	Physical assessment findings of skin tenting (new or worse), dry mucus membranes, OR symptomatic orthostasis (new and not explained by medication)	5 (3%)	4 (3%)	9(3%)
Hypernatremia	Serum sodium above 140.0 mEq/L	4 (3%)	4 (3%)	8 (3%)
Hyperkalemia	Serum potassium levels exceed 5.3 mmol/l,	1 (1%)	1 (1%)	1 (1%)
Hypokalemia	Serum potassium less than 3.5 mmol/l	1 (1%)	0 (0%)	1 (1%)
Hyperthyroid	Reflex T4 less than 0.4	4 (3%)	2 (1%)	6 (2%)
Hypothyroid	Reflex T4 higher than 5.5	5 (3%)	2(1%)	7 (2%)
TOTALS	Subjects with one or more detected illnesses in sample	56 (35%)	40 (37%)	96 (36%)

KEY:

^a Advancing Caregiver Training (Project ACT)^b Care of Persons with Dementia in their Environment (Project COPE)

Table 2

Comparison of Demographic Characteristics of ACT and COPE Samples

	ACT Sample (n=158)	COPE Sample (n = 117)	χ^2	Z
Characteristic Mean (SD)				
<u>Dementia Subject</u>				
Age	82.3 (8.5)	83.3 (7.6)		-0.72
Gender (%)			17.84**	
Male	53.0	23.2		
Female	47.0	76.8		
Race (%)			1.8	
White	65.8	74.4		
AA	34.2	24.8		
Number of behaviors	9.4 (3.7)	10.6 (4.2)		-2.13
Functional status (ADL)	4.0 (1.8)	4.3 (1.7)		-1.03
MMSE	12.8 (8.1)	13.5 (8.0)		-0.4
<u>Caregiver</u>				
Age	67.1 (11.7)	63.2 (12.6)		-0.50
Race (%)			5.25	
White	68.5	74.4		
AA	34.2	25.6		
Gender (%)			.32	
Male	18.8	14.5		
Female	81.2	85.5		
Relation to CR (%)			7.46**	
Spouse	51.3	30.8		
Non-spouse	48.7	69.2		
Education (%)			19.38**	
< High School	7.7	36.8		
High School	29.9	24.8		
> High School	62.4	38.5		
Years caregiving	3.9 (3.1)	4.0 (4.4)		-0.15

Note:

**
p<.01

Table 3

Differences between Persons with Dementia with Detected Acute Illness and Those with No Evidence of Acute Illness (N=265)

Characteristic	No Evidence of Acute Illness N=179	Evidence of Acute Illness N=96	X2	T	P
Mean Age (mean, SD)	81.56 (8.5)	83.4 (8.7)		1.34	.12
Gender (Female, %)	64%	77%	1.57		.22
Race (White, %)	72%	71%	1.67		.13
Married, %	51%	59%	1.69		.10
Functional Status (mean, SD)	4.41 (1.7)	3.82 (1.5)		7.03	.01
MMSE (mean, SD)	14.4 (7.9)	10.5 (8.0)		12.1	.001
Number of Behaviors	9.45 (4.1)	9.58 (4.2)		.058	.81
Psychotropic Medications (%yes)	36%	41%	3.67		.049

Note: MMSE = Mini Mental State Exam score

Table 4

Bivariate Analysis of Detected Acute Illness and Neuropsychiatric Behaviors for total sample (N= 265)

Illness	Neuropsychiatric Behavior	<i>Phi</i>[*]
Bacteriuria	Incontinence	.174 ^{**}
	Agitation	.124 ^{**}
Hyperglycemia	Repeated questioning	.108
	Agitation	.102
Anemia	Crying out	.108
Metabolic disorder	Agitation	.128 ^{**}
	Delusion	.124 ^{**}
	Hallucinations	.107

*
p<.05 unless otherwise indicated**
p<.01