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# Cohort and epidemiological studies

## FTD

### 1.1.1 Armstrong et al. (2013) – Caregiver burden in frontotemporal degeneration and corticobasal syndrome.

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| Reference | Armstrong, Nicole; Schupf, Nicole; Grafman, Jordan; Huey, Edward D. (2013): Caregiver burden in frontotemporal degeneration and corticobasal syndrome. In *Dementia and geriatric cognitive disorders* 36 (5-6), pp. 310–318. DOI: 10.1159/000351670. |
| Type | Controlled cohort study, descriptive study |
| Location/Country | USA |
| Aim/subject | To assess the association between behavioral symptoms and caregiver burden in frontotemporal dementia (FTD) and corticobasal syndrome (CBS) |
| Participants (number, patient diagnosis, gender, age range, race, ethnicity, type of residency [home, care facility], initial treatment, caregiver relationship to patient, initial scores) | 267 caregivers of FTD/CBS patients in total who received questionnaires (n = 180 FTD caregivers, n = 87 CBS caregivers)FTD/CBS diagnosis confirmed at National Institutes of Health according to published consensus criteria102 caregivers completed FrSBe and ZBI (n = 61 FTD caregivers, n = 41 CBS caregivers)Age of patient: FTD 60±9; CBS: 66±8; total: 63±9Gender of patient: FTD 30 male/31 female; CBS 21 male/20 female; (total 51 male/51 female)Race of patient: FTD 60 white/Caucasian, 1 other; CBS 37 white/Caucasian, 2 African American, 2 Asian/Pacific IslandersCaregiver relationship to patient: FTD 53 significant other, 8 family members; CBS 34 significant other, 5 family members, 1 friend, 1 paid caregiver |
| Methods/measures | FrSBe – T-score used as main predictor variable, representing frontal lobe dysfunction (≥ cutoff score 65), adjusted for gender, level of education and ageZBI – total score used as main outcome variable, representing caregiver burden (> cutoff score 24)Multivariate regression model using T-score, ZBI score, relationship to patient and diagnosisT-scores from apathy and disinhibition subscales of the FrSBe examined separately as independent predictorsAssociations between groups of (1) caregivers of patients with apathy and disinhibition, (2) caregivers of patients with only apathy, (3) caregivers of patients with only disinhibition and (4) caregivers of patients without either apathy or disinhibition examined by one-sample t testAssociations regarding type of diagnosis examined by between-group two-sample t testRelationship to patient and type of diagnosis considered as potential confounders |
| Interventions (where applicable) | none |
| Outcomes (variables, main findings) | Caregiver burden = ZBI scoresFrontal Lobe Dysfunction = FrSBe T-scoresCaregivers of patients with frontal lobe dysfunction had 13.0 times the odds of experiencing caregiver burden than caregivers of patients without frontal lobe dysfunctionAssociation between apathy and disinhibition subscales of the FrSBe to caregiver burden - 57 patients exhibited both apathy and disinhibitionExecutive dysfunction subscale of FrSBe not considered as a covariate since sample homogenous in attaining scores ≥65Apathy and disinhibition can co-occur; apathy can occur without disinhibition whereas disinhibition without apathy is very rare |
| Limitations | FTD subtypes were not considered separately due to small patient numbersFrSBe narrow in scope – some symptoms that are included in the NPI are not measuredNo information about dementia severity in patients availableNo information about caregiver characteristics (e.g. age, gender) availableNo control/comparison group |

### 1.1.2 Ascher et al. (2010) – Relationship satisfaction and emotional language in frontotemporal dementia and Alzheimer’s disease patients and spousal caregivers.

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| Reference | Ascher, Elizabeth A.; Sturm, Virginia E.; Seider, Benjamin H.; Holley, Sarah R.; Miller, Bruce L.; Levenson, Robert W. (2010): Relationship satisfaction and emotional language in frontotemporal dementia and Alzheimer disease patients and spousal caregivers. In: *Alzheimer disease and associated disorders* 24 (1), S. 49–55. DOI: 10.1097/WAD.0b013e3181bd66a3. |
| Type | Controlled comparative study, descriptive study |
| Location/country | California, USA  |
| Aim/subject | To assess the impact of Alzheimer’s disease (AD) and Frontotemporal dementia (FTD) on marital satisfaction and the use of emotional language in comparison with control group (CG) couples |
| Participants  | 52 male-female couples, one partner either being a dementia (FTD or AD) patient or a healthy control respectively with their spousal caregivers or spouses, respectively; 15 FTD couples, 16 AD couples, 21 CG couplesFTD and AD patients recruited as referrals to the Memory and Ageing Center (MAC) of the University of California, San Francisco, diagnosis made by MAC staff early-onset AD couples recruited in order to equalize ageCG couples recruited through local community advertisement, neurological and psychiatric health confirmed at MACSpouse or partner had to be willing to participateControl patient = patient analogs, control caregiver = caregiver analogsAge of patient: FTD mean 60.37 (SD 6.09); AD mean 59.28 (SD 5.28); CG mean 66.58 (7.88); total mean 62.08 (SD 0.93)Gender of patient: FTD 13 male/2 female; AD 10 male/6 female; CG 15 male/6 female; total 38 male/14 femalePatient CDR box score (dementia severity, range 0-18): FTD mean 6.93 (SD 0.51); AD mean 4.56 (SD 0.50); CG mean -0.09 (SD 0.45); total mean 3.80 (SD 0.27)Age of caregiver: FTD mean 56.90 (SD 7.60); AD mean 54.02 (SD 7.03); CG mean 64.03 (SD 6.60); total mean 58.31 (SD 0.99)Gender of caregiver: FTD 2 male/13 female; AD 6 male/10 female; CG 6 male/15 female; total 14 male/38 femaleAge of couple: FTD mean 58.64 (SD 1.53); AD mean 56.65 (SD 1.48); CG mean 65.30 (SD 1.30) |
| Methods/measures | Clinical Dementia Rating Scale (CDR): to assess dementia severity, administered by MAC staff, CDR box score = sum of subscores from 6 domains of daily functioning, range 0-18Locke-Wallace Marital Adjustment Scale: self-report 15-item questionnaire administered to both partners of each couple, score range 2-158; score <100: dissatisfied couples, ≥100: satisfied couplesAll couples underwent a battery of tasks assessing emotional functioning, including a social interaction task that was used to examine the use of emotional languageSocial interaction task: 15-minute conversation about an area of conflict in partnership, topic was chosen in advance with guidance of an experimenter, partners seated facing each other, 5-minute silent period before start of conversation, audio and video recording of the situation, only audio records used hereAudio record transcribed, transcripts were analyzed using a text analysis programme that compared words used to words of an emotion dictionary, word and context presented to coder who was blind to grouping in order to eliminate context-related non-emotional homonyms from countingEmotional word dictionary: words that refer to an emotional state, 1500 words in the superordinate categories of ‘positive’ and ‘negative’, positive words being subdivided into 12 categories, negative words into 15 categoriesNumber of positive emotion words, negative emotion words and total number of words used were computed for each speaker |
| Interventions | none |
| Outcomes | No significant differences in proportions of caregiver and patient sex; CG couples significantly older than FTD and AD couples (FTD and AD couples did not differ in age), caregivers younger than patients across all groups; AD patients were less impaired by their dementia than FTD patients, CG was less impaired than both dementia groups; differences found both in age and dementia severity 🡪 used as covariates for subsequent analysesMarital satisfaction: FTD couples significantly exhibit a significantly lower level of marital satisfaction (Locke-Wallace mean 88.22, SD 6.72, indicating a dissatisfied couple) than AD couples (Locke-Wallace mean 117.92, SD 4.74) and CG couples (Locke-Wallace mean 124.12, SD 6.11); AD and CG couples did not differ significantly, both Locke-Wallace mean scores indicating a satisfied coupleEmotional language: FTD caregivers used significantly more negative emotional language than FTD patients, AD caregivers used significantly more negative emotional language compared to AD patients; however, in comparison with FTD this difference was not significant anymore; no significant differences in use of negative emotional language in CG patients and partners; FTD caregivers used significantly more negative emotional language than AD and CG caregivers (no significant difference between AD and CG caregivers), no significant difference in use of negative emotion language among patients of all three groupsIn the use of positive emotional language, no significant differences could be foundThere was no significant lack of positive emotional language in FTD couples, FTD diagnosis however has an extensive influence on marital satisfaction; hypothesis that FTD patients are unaware of low marital satisfaction and tend to overestimate it were not proven, also AD patients did not minimize marital problems |
| Limitations | Control group was significantly olderEarly-onset AD patients may not represent the AD population in generalNo longitudinal development of marital problems assessedAbility to reliably self-report marital satisfaction might be difficult in severely impaired dementia patients |

### 1.1.3 Boutoleau-Bretonniere et al. (2008) – Zarit burden inventory and activities of daily living in the behavioral variant of frontotemporal dementia.

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| Reference | Boutoleau-Bretonniere, Claire; Vercelletto, Martine; Volteau, Christelle; Renou, Pierre; Lamy, Estelle (2008): Zarit burden inventory and activities of daily living in the behavioral variant of frontotemporal dementia. In: *Dementia and geriatric cognitive disorders* 25 (3), S. 272–277. DOI: 10.1159/000117394. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Nantes, France |
| Aim/subject | To assess activities of daily living (ADL) and caregiver burden in FTD in comparison with early-onset Alzheimer’s Disease (AD) and examine between-scale correlations |
| Participants | Patients attending Neurological Memory Center at Nantes University Hospital were enrolled over a 18-month period of time, examination by neurologist and neuropsychologist, MRI and SPECT imaging supporting diagnosis; Inclusion criteria: AD patients with diagnosis according to NINCDS-ADRDA criteria, FTD patients with diagnosis according to Neary criteria for bvFTD, age range of 50-75 years (in order to obtain comparable results, meaning early-onset AD patients were recruited), caregiver who saw patient on a regular basisExclusion criteria: institutionalized patients, lack of principal caregiverDiagnosis of patient: AD n = 28, FTD n = 26Age of patient: AD mean 63.3 (SD 6.2, median 63.5), FTD mean 65.7 (SD 7.4, median 68)Gender of patient: AD 12 male/16 female; FTD 16 male/10 femaleYears of education of patient: AD mean 8.3 (SD 3.7, median 6); FTD mean 8.2 (SD 3.9, median 6) Months of disease evolution in patient: AD mean 47.2 (SD 25.3, median 48); FTD mean 52.8 (SD 55.6, median 36)Age of caregiver: AD mean 62.2 years (SD 8.8); FTD mean 60.2 (SD 8.3)Sociocultural level of caregiver: AD mean 9.6 (SD 3.2), FTD mean 9.1 (SD 3.6)  |
| Methods/measures | Cognitive function: assessed using the Mini Mental State Exam (MMSE), score range 0-30, higher scores indicating better cognitive function, cut-off score in use not reported hereassessed by Mattis Dementia Rating Scale (MDRS), score range 0-144, higher scores indicating better cognitive function, cut-off score in use not reported hereBehavioral impairment: assessed using the Neuropsychiatric Inventory (NPI), score range 0-144, higher scores indicating greater behavioral impairment, scores obtained by an interview with caregiver and behavioral assessments of the previous 4 weeks, cut-off score in use not reported hereFunctional disability: assessed using the Disability Assessment for Dementia (DAD), score range 0-100% of maximum score of 40; the three patterns of initiation, planning/organization and effective performance are evaluated for basic, instrumental and leisure activities using caregiver observations of the previous 2 weeksCaregiver burden: assessed using the Zarit Burden Interview (ZBI), score range 0-88, French validated ZBI version, administered during an interview, suggested scores (for AD) used: ≤20 little or no burden, 21-40 mild to moderate, 41-60 moderate to severe, ≥61 severe burden |
| Interventions | none |
| Outcomes | Patient groups did not differ significantly in age, level of education, MMSE score or evolution of disease; no significant difference in caregiver age and sociocultural levelFTD patients obtained significantly higher NPI score than AD patientsZBI score was significantly higher for FTD than for AD caregiversZBI correlated with NPI in both AD an FTD patients (in the latter, this correlation was significant)ZBI correlated significantly with MDRS in AD patientsZBI did not correlate significantly with DAD scoresNo correlation between DAD and MDRS or DAD and NPINo correlation between initiation subscale of MDRS and DADNo differences between groups in DAD and its sub-scoresNPI domains of apathy, aberrant motor behavior and appetite and eating abnormalities were highest in FTD patients, NPI domains of apathy, aberrant motor behavior and night-time behavior disturbance highest in AD group;highly significant difference between both groups in domains of apathy, disinhibition, appetite and eating abnormalitiesDegree of independence in daily life very similar between AD and FTD patients matched in terms of cognitive level, no correlation could be found between ADL and behavioral impairment, higher caregiver burden in FTD caregivers is more likely to be based on behavioral impairment than on impairment in ADL  |
| Limitations | Small sample sizeEarly-onset AD patients may not represent the AD population in generalLack of information about caregiver characteristics (e.g. gender)MMSE is considered insensitive in FTD cognitive decline (Piguet et al. 2013) |

### 1.1.4 Brioschi Guevara et al. (2015) – Theory of mind impairment in patients with behavioral variant fronto-temporal dementia (bv-FTD) increases caregiver burden.

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| Reference | Brioschi Guevara, Andrea; Knutson, Kristine M.; Wassermann, Eric M.; Pulaski, Sarah; Grafman, Jordan; Krueger, Frank (2015): Theory of mind impairment in patients with behavioral variant fronto-temporal dementia (bv-FTD) increases caregiver burden. In: *Age and ageing* 44 (5), S. 891–895. DOI: 10.1093/ageing/afv059. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Maryland, USA |
| Aim/subject | To assess the effect of Theory of Mind (ToM) impairments in bvFTD patients on caregiver burden, to assess the association of regional brain atrophy with ToM impairment and caregiver burden |
| Participants | bvFTD patients n = 28, subgroup of their caregivers n = 20, healthy controls (HC) n = 18 who completed the faux-pas (FP) task for ToM evaluation (HC-FP), HC group n = 14 who underwent MRI scan (HC-MRI) bvFTD, HC-FP and HC-MRI groups matched on age, gender and educationAge of patient: bvFTD mean 59.18 years (SD 1.79), HC-FP mean 60.33 (SD 2.07), HC-MRI mean 60.57 (SD 1.70)Education of patient: bvFTD mean 15.89 years (SD 0.64), HC-FP mean 15.08 (SD 0.39), HC-MRI mean 17.14 (SD 0.93)Gender of patient: bvFTD 20 male/8 female, HC-FP 8 male/10 female, HC-MRI 7 male/7 femaleNational Adult Reading Test (NART, see below): bvFTD mean 28.61 (SD 1.43), HC-FP mean 37.39 (SD 1.93)Mattis Dementia Rating Scale (DRS-II, see below): bvFTD mean 4.57 (SD 0.57), HC-FP mean 12.00 (SD 0.47) |
| Methods/measures | Cognitive function: assessed using the Mattis Dementia Rating Scale (DRS-II), scaled score, higher scores indicating better cognitive performanceIntelligence: assessed using the National Adult Reading Test (NART), participants are asked to pronounce 50 words, higher scores indicate greater intelligence (strong correlation with Wechsler Adult Intelligence Scale-IQ in the bvFTD group)Theory of Mind performance: assessed using a faux-pas (FP) task in which participants read short stories and are asked to answer whether somebody in the story said something inappropriate (FP questions) and control questions to verify that the participant had understood the story, percentages were calculated for both types of questions (FP score = FPS and control score = CS)Caregiver burden: assessed using the Zarit Burden Interview (ZBI) overall score, i.e. the last item that rates the overall burden with a score range of 0 (not at all burdened) to 4 (extremely burdened)Neuroimaging: T1-weighted MRI obtaining voxel-based morphometry of the brain, yielding: total intracranial volume (TIV), ventricular size, grey matter and white matter compared between bvFTD and HC-MRI groups using independent-samples *t*-tests linear regression to examine relationship between bvFTD FP performance and regions of brain atrophy  |
| Interventions | None |
| Outcomes | bvFTD group performed significantly worse in cognition (DRS-II) and intelligence (NART) tasks compared to HC-FPFP task: FP performance not associated significantly with intelligence or gender, but main effects for condition (FPS, CS) and group; significant interaction between FP performance and condition × groupFollow-up one-way ANCOVAs on FP performance with group as a between-subjects factor and gender and intelligence as covariates showed no group differences in CS, but for FPS 🡪 bvFTD group more impaired in FPS, but not in CSSignificant positive association between caregiver burden and FPSNeuroimaging: grey matter and white matte volumes significantly reduced in bvFTD patients compared to HC-MRI group, reverse effect in ventricular size; linear regression showed significant association between FP performance and the dorsolateral prefrontal cortex (dlPFC), right orbitofrontal cortex (OFC), left lateral premotor cortex (PMC), left medial PMC and left superior temporal cortex (STC)significant association between caregiver burden and voxel density in the left lateral PMC (greater atrophy correlates with greater caregiver burden)ToM impairment indicates difficulties in social interactions with bvFTD patients, thus leading to greater distress for caregiversAtrophy in the PMC – which is associated with caregiver burden - indicates a decline in preparation of actions and together with the dlPFC is associated with goal-directed behaviors |
| Limitations | Association between ToM, brain areas and caregiver burden might be influenced by other factors not considered or not controllable in the study Atrophy of PMC associated with burden is speculativeOther architectural properties of the brain (e.g. cortical thickness) were not investigatedDifferent control groups used for FP task and neuroimagingOnly overall burden item used for determining caregiver burden instead of the entire ZBISmall sample sizeNo information about caregiver characteristics (e.g. age, gender) available |

### 1.1.5 Bristow et al. (2008) – Stress, distress and mucosal immunity in carers of a partner with frontotemporal dementia.

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| Reference | Bristow, Matt; Cook, Rachel; Erzinclioglu, Sharon; Hodges, John (2008): Stress, distress and mucosal immunity in carers of a partner with fronto-temporal dementia. In: *Aging & mental health* 12 (5), S. 595–604. DOI: 10.1080/13607860802343076. |
| Type | Controlled cohort study, descriptive study |
| Location/country | United Kingdom |
| Aim/subject | To assess the physiological and psychological impact on caregiving for FTD patients on spousal caregivers using psychological assessments as well as measuring the mucosal immunity as a marker of stress level |
| Participants | 25 caregivers providing care for a spouse or partner recruited from a local support group, 36 non-carer controls (CG) recruited from a research participant panelDiagnosis of patient: 11 frontal variant FTD, 14 semantic variant FTD – one patient’s diagnosis changed from semantic variant FTD to AD, caregiver psychosocial data was excluded from analysis, mucosal immunity data was used nonethelessAge of caregiver (years): caregiver mean 62.9 (±5.9); CG mean 63.3 (±5.4)Gender of caregiver: caregiver 6 male/19 female, CG 11 male/25 femaleEmployment status: caregiver 3 full-time/4 part-time/17 retired/1 unemployed; CG 3 full-time/11 part-time/19 retired/1 unemployed/2 otherOther dependents to care for: caregiver 23 none/2 one; CG 34 none/1 one/1 twoSocioeconomic status reported |
| Methods/measures | *Recent functioning questionnaire*Psychological distress: assessed using the General Health Questionnaire (GHQ-30), sub-scores for well-being, lack of self-esteem and sociability, tension, and freedom from tensionPerceived stress: assessed using the Perceived Stress Scale (PSS)Social support: assessed using the Significant Others Scale (SOS), scores for satisfaction with practical support and satisfaction with emotional support, over the past 6 monthsCaregiver burden: assessed using the Caregiver Burden Scale (CBS); sub-scores for objective burden, subjective demand burden, subjective stress burdenCoping strategies: assessed using the Ways of Coping (Revised) with eight subscalesCompleted at time convenient for caregiver*Daily functioning questionnaire*Daily stress and arousal: assessed using the Stress-Arousal Checklist (SACL)Positive and negative mood: assessed using a 12-item checklistCompleted on three consecutive weekdays together with IgA sample*Mucosal immunity stress level test*Participants were asked to take a saliva sample by placing a cotton wadding in their mouth for two minutes on three consecutive weekdays, cooling and transportation of saliva samples were ensured to be compliant with research requirements; only the last valid sample was used because in many cases there was no sufficient amount of saliva in all three samples; three carers and one CG participants were excluded due to infectious illnesses, one CG participant was excluded because all his IgA levels were higher than three SDs above the meanIgA was analyzed using a commercial kit, all IgA values reported as secretion rate µg/min |
| Interventions | None |
| Outcomes | Caregivers reported significantly higher perceived stress on the PSS, higher daily stress and lower positive mood when compared to CG, psychological distress was significantly higher in caregivers as well as a lack in self-esteem, well-being and freedom from tension on the GHQ-3050% of caregivers met criteria for a psychiatric disorder on the GHQ-30 as compared to 16.6% CG participants.No difference in arousal or negative mood between groupsNo differences between groups in the fields of satisfaction with emotional support and satisfaction with practical support, however, post-hoc t tests revealed that the dissatisfaction of both practical and emotional support was greater in the caregiver group with the first person in their social network (usually the person being cared for)Caregiver perceived stress was correlated with all three caregiver burden subscales; positive GHQ-subscales freedom from tension and positive well-being were negatively associated with all three caregiver burden subscalesPositive correlation between negative GHQ-subscales and subjective stress. No distress, stress or burden differences between caregivers of fvFTD and SD.No reduced IgA secretion was found in caregivers; an unexpected finding was the positive correlation between IgA secretion and perceived stress as well as psychological distress in the caregiver group; no such associations in the CG |
| Limitations | IgA levels vary and respond differently to acute stress than to chronic stressOnly one sample per person could be used contrary to the intended 3-day sample overviewSmall sample sizeSelection of spousal caregivers – no representation of other caregivers, e.g. children and their stress level |

### 1.1.6 Brodaty et al. (2014) – Prevalence and predictors of burden in caregivers of people with dementia.

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| Reference | Brodaty, Henry; Woodward, Michael; Boundy, Karyn; Ames, David; Balshaw, Robert (2014): Prevalence and predictors of burden in caregivers of people with dementia. In: *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry* 22 (8), S. 756–765. DOI: 10.1016/j.jagp.2013.05.004. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Australia |
| Aim/subject | To assess prevalence and predictors of caregiver burden in caregivers of patients with different types of dementia attending memory clinics |
| Participants | Recruitment in one of nine memory clinics in Australia, part of the PRIME (Prospective Research in Memory Clinics) cohort, between August 2005 and July 2011Dementia patients with Alzheimer’s Disease (AD), Vascular dementia (VaD), FTD or mixed dementia (AD and VaD)Inclusion criteria: dementia diagnosis according to DSM-IV or mild cognitive impairment by the Petersen criteria, living in the community with less than 40h/week nursing care, caregiver willing to provide consent, fluency in English, provision of informed consent through the patient themselves or guardian/proxyExclusion criteria: concomitant life-threatening illness affecting patient’s ability to complete the study, current participation in a clinical trial of an investigational drug (phase I, II or III), diagnosis of mild cognitive impairment *and* prescription of a cholinesterase inhibitor or memantineTotal sample of 732 participants of which 577 completed the duration of the study of 12 months, 86 patients having discontinued by the 6-month follow-up and 69 patients having discontinued by the time of the 12-month follow-up (total number of dropouts: 155)Total sample baseline characteristics of patients:Diagnosis of patient: AD 521 (71.2%), VaD 51 (7.0%), FTD 31 (4.2%), mixed 129 (17.6%)Mean age of patient: 78.3 (SD 7.4)Gender of patient: 372 (50.8%) male/360 (49.2%) femaleMean age at symptom onset: 74.3 (SD 8.2)Living arrangement: with spouse 545 (74.5%), alone 93 (12.7%), other 94 (12.8%)Living at home: 712 (97.3%)Driving: 229 (31.3%)Use of resources (i.e. medical resources such as family doctor, specialist): 271 (37.0%)Use of psychotropic medication: 262 (35.8%)Use of cholinesterase inhibitors: 575 (78.6%)Caregiver characteristics:Gender of caregiver: 257 (35.1%) male/475 female (64.9%)Relationship to patient: spouse 521 (71.2%), child 159 (21.7%), other 52 (7.1%)Employed: 172 (23.5%)Used resources (i.e. caregiver support resources): 94 (12.8%)  |
| Methods/measures | Follow-up at 6 and 12 months’ time after enrollmentCognitive impairment: - assessed using the Clinical Dementia Rating Scale (CDR), score range 0-3, a score of 3 indicating severe dementia- assessed using the Mini Mental State Exam (MMSE), score range 0-30, lower scores indicating greater cognitive impairment- assessed using the Alzheimer’s Disease Assessment Scale-Cognitive (ADAS-Cog, particularly for patients with MMSE scores ≥25), score range 0-70, higher scores indicating greater cognitive impairmentFunctional disability: assessed using the Functional Autonomy Measurement System (SMAF), score range 0 to -87, lower scores indicating greater functional disability and thus dependenceBehavioral impairment: assessed using the Neuropsychiatric Inventory (NPI), score range 0-144, higher scores indicating greater behavioral disturbancesCaregiver burden: assessed using the Zarit Burden Interview (ZBI), score range 0-88, score 21-40 = mild to moderate burden, ≥41 = moderate to severe burdenTesting instruments, demographics, use of resources in patients and caregivers were recorded at baseline and subsequent visits, each item was recommended but not required to be completed |
| Interventions | None |
| Outcomes | Drop-outs were older, older at the age of onset, had more severe dementia, greater functional disability, greater behavioral impairment, less likely to be driving and less well educated, caregivers had higher baseline ZBI, sensitivity analysis yielded a regression model that showed similar results, indicating that drop-outs did not significantly influence the findingsSignificant caregiver burden (ZBI ≥21) increased from 50% to 57.7% at 12 months, severe burden (≥41) increased from 14.7% to 22.8%, use of caregiver resources did not change (12.7% to 12.8%)Patients showed a worsening of cognitive impairment, greater dependence and greater behavioral impairment Predictors at 6 months: univariate analysis showed significant association between ZBI score and FTD diagnosis, longer duration of dementia, lower MMSE score, higher CDR score, lower SMAF score, higher NPI frequency score, living alone, use of antidepressants, use of antipsychotics, female caregiverStepwise regression model contained three predictor variables: baseline ZBI score, antipsychotic use, baseline MMSE scorePredictors at 12 months: univariate analysis showed significant association between ZBI score and FTD diagnosis, living alone, longer duration of dementia, lower MMSE score, higher CDR score, lower SMAF score, higher NPI frequency score, antidepressant use, antipsychotic use, female caregiverStepwise regression model contained five predictor variables: antipsychotic use, antidepressant use, MMSE score, NPI score, ZBI scoreRepeated analysis of predictors including changes in MMSE and SMAF scores showed that FTD diagnosis, baseline ZBI, use of antipsychotics and antidepressants remained variables, but decline in functional abilities (SMAF) was strongly associated with 12-month burdenFemale caregivers reported higher burden than male caregivers even accounting for the higher occurrence of behavioral and psychological symptoms in dementia (BPSD) in male dementia patients |
| Limitations | Lack of information about caregiver characteristics (e.g. gender)Use of MMSE in FTD patients questionable (Piguet et al. 2013) |

### 1.1.7 Chow et al. (2011) – An international needs assessment of caregivers for frontotemporal dementia.

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| Reference | Chow, Tiffany W.; Pio, Fabricio J.; Rockwood, Kenneth (2011): An International Needs Assessment of Caregivers for Frontotemporal Dementia. In: *Can. J. Neurol. Sci* 38 (05), S. 753–757. DOI: 10.1017/S0317167100054147. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Multi-national: Canada, USA, UK and Europe |
| Aim/subject | To assess the needs of FTD caregivers and their aspects considered to be important in FTD. |
| Participants | Recruitment from mailing list for FTD caregivers initiated by co-author – mailing list was established at clinics and lectures those participants were asked to invite other caregivers they know; inclusion criteria: self-identified caregiver for a person with FTD, English-speaking, internet access sufficient to complete online survey78 respondents to the first question, 62 completed the entire surveyLocation of respondents (completed by 64): 31 from Canada, 20 from the USA, 13 from UK and Europe Gender of respondents (n=63): 26 male/37 femaleAge of respondent: median 58 years (range 28-78)Diagnosis of patient cared for (n=78, multiple answers): 22 bvFTD, 21 SD, 14 PNFA, 14 no diagnosis yet, 13 CBS, 12 ALS-FTD, 6 logopenic progressive aphasia, 4 atypical AD, 3 Parkinson’s, 2 progressive supranuclear palsy |
| Methods/measures | Online survey accessible after creation of a login, anonymized dataQuestions regarding- diagnosis of patient (multiple possible answers)- first symptom noted by the caregiver (one possible answer)- most troublesome aspects of caregiving (up to three possible answers)\*- most helpful resource or intervention (one possible answer)\*- biggest surprise in learning about FTD (one possible answer)\*- demographic data: country, zip/postal code, gender, year of birth (optional questions)\*Fill-in-the-blank options available for other responses besides those listed |
| Interventions | None |
| Outcomes | Most caregivers first noted a change in thinking and judgment, followed by memory and behavior changesMost troublesome aspects were not knowing that the patient was suffering from a dementia or some other kind of neurological impairment, difficulty in obtaining a diagnosis and not knowing how to help the patientThe resources being most helpful were the neurologist, information from the internet and help from their own children.For most caregivers, it was unexpected to find out that dementia can affect young people, that they discovered strength in dealing with the problem and that symptoms fluctuate |
| Limitations | Recruitment included participants who already sought information, those without internet access were excludedDue to word-of-mouth recruitment, some caregivers may provide care for the same patientFTD subtypes were not analyzed separately (multiple diagnoses could be stated)Missing answers |

### 1.1.8 Cosseddu et al. (2013) – The other face of the coin. The caregiver burden in frontotemporal lobar degeneration.

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| Reference | Cosseddu, Maura; Alberici, Antonella; Pelizzola, Sabrina; Padovani, Alessandro; Borroni, Barbara (2013): The other face of the coin. The caregiver burden in frontotemporal lobar degeneration. In: *International journal of geriatric psychiatry* 28 (6), S. 655–657. DOI: 10.1002/gps.3892. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Brescia, Italy |
| Aim/subject | To assess caregiver burden, health-related quality of life (HQoL), depression and anxiety in caregivers of FTLD patients |
| Participants | 56 FTLD patients and their caregivers Diagnosis of patient: 39 bvFTD, 17 primary progressive aphasia (PPA)Age of patient: mean 67.4 years (range 48-83)Gender of patient: 64.3% male/35.7% femaleDisease duration: mean 4.2 yearsAge of onset: mean 63.1 years (range 46-81)Eight patients (5 bvFTD, 3 PPA) carried granulin pathogenic mutationsAge of caregiver: mean 57.9 years (range 30-72)Gender of caregiver: 25% male/75% femaleRelationship to patient: 73.2% spouses, 26.8% children |
| Methods/measures | Caregiver interviewsHealth-related quality of life (HQoL): assessed using the Short Form 36 survey (SF-36) including the Mental Component Summary and the Physical Component Summary (MCS and PCS)Caregiver burden: assessed using the Caregiver Burden Inventory (CBI)Depression: assessed using the Zung Self-Rating Depression ScaleAnxiety: assessed using the State-Trait Anxiety InventoryNo information about score ranges and cutoff scores provided |
| Interventions | None |
| Outcomes | Caregiver HQoL: caregiver’s increased age was associated with worse PCS scores; PCS scores related to bvFTD diagnosis, male gender of patient, absence of *GRN* mutation; stepwise multiple regression showed independent correlation of patients’ male gender and bvFTD diagnosis to PCS scores;severity of behavioral symptoms (assessed using the Frontal Behavioral Inventory [FBI] total score) was associated with worse MCS scoresCaregiver burden: CBI scores significantly associated with bvFTD diagnosis and FBI total scores; stepwise multiple regression showed that FBI total scores were independently related do CBI scoresCaregiver depression: Self-rating Depression scale scores correlated significantly with caregiver relationship – spouses were more depressed than other caregiversCaregiver anxiety: State-Trait Anxiety Inventory scores were significantly associated with FBI scores No association found between CBI scores and genetic status, positive family history, disease duration or age of onset |
| Limitations | Scarce information about assessment administered to patientsNo control/comparison group |

### 1.1.9 Davis and Tremont (2007) – Impact of frontal systems behavioral functioning in dementia on caregiver burden.

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| Reference | Davis, Jennifer Duncan; Tremont, Geoffrey (2007): Impact of frontal systems behavioral functioning in dementia on caregiver burden. In: *The Journal of neuropsychiatry and clinical neurosciences* 19 (1), S. 43–49. DOI: 10.1176/jnp.2007.19.1.43. |
| Type | Controlled comparative study, descriptive study |
| Location/country | USA |
| Aim/subject | To assess the impact of frontal systems behavioral functioning on caregiver burden in dementia. |
| Participants | Recruitment from community and memory clinicsInclusion criteria: patient living at home with the caregiver, care for min. 4h/day for at least 6 months; dementia confirmed by physician, dementia severity assessed by CDR via phone interviewn=72Diagnosis of patient: 42 AD, 4 vascular dementia, 4 mixed dementia, 5 FTD, 4 LBD, 3 Parkinson’s disease, 2 hydrocephalus, 1 PSP, 2 dementia not otherwise specified, 5 unknownDementia severity: 47 mild/25 moderateAge of patient: mean 77.18 (±9.47)Age of caregiver: mean 64.36 (±11.66)Gender of caregiver: 16 male/56 femaleMajority Caucasian; majority spouses of the patientCaregiving: mean 18.24h (±7.19) of daily contact; care provided for average 39.68 months (±35.57); time since dementia diagnosis mean 39.71 months (±35.90) |
| Methods/measures | Self-reported questionnaires as part of a baseline assessment of an interventional studyBehavior: assessed using the Frontal Systems Behavior Scale (FrSBe), three subscales, raw overall score converted into adjusted t-scoresADL: assessed using the Activities of Daily Living Questionnaire (ADL), basic and instrumental ADLs, score range 0-28, higher scores indicating higher functional independenceCaregiver burden: assessed using the Zarit Burden Interview (ZBI), score range 0-88, higher scores indicating a higher burdenDepression: assessed using the Geriatric Depression Scale (GDS), higher scores indicating more depressive symptoms |
| Interventions | None |
| Outcomes | Caregiver burden is moderately associated with caregiver depression and behavioral problemsTotal ADL scores were moderately associated with caregiver burdenIn regression analysis, ADL, GDS scores and FrSBe ‘after onset’ scores accounted significantly for variance in ZBI scoresIn a second regression analysis, FrSBe ‘after’ scores accounted significantly for ZBI scores, sub-scores of executive dysfunction and disinhibition were significant predictors for ZBI scoresADL and FrSBe ‘before onset’ scores accounted significantly for the variance of GDS scoresDementia subtypes were grouped into ‘Alzheimer’s disease’ and ‘other dementia types’ – no differences were found in resultsSpousal and adult child caregivers were compared, dementia severity was higher in care recipients of child caregivers, no other differences were found |
| Limitations | No objective measure on executive dysfunctionNo differentiation of all dementia subtypes in analysesSelf-reported measured may impair objectivityFemale caregivers overrepresentedNo patients with severe dementia included |

### 1.1.10 Denny et al. (2012) – Caring for children of parents with frontotemporal degeneration: a report of the AFTD Task Force on Families With Children.

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| Reference | Denny, Sharon S.; Morhardt, Darby; Gaul, J. Elise; Lester, Paul; Andersen, Gail; Higgins, Paul J.; Nee, Linda (2012): Caring for children of parents with frontotemporal degeneration: a report of the AFTD Task Force on Families With Children. In *American journal of Alzheimer's disease and other dementias* 27 (8), pp. 568–578. DOI: 10.1177/1533317512459791. |
| Type | Study report |
| Location/country | USA |
| Aim/subject | To report the results of a task force aimed at the care for children of patients with FTD |
| Participants | 7-person task force: program director of the Association for Frontotemporal Dementia (AFTD), 2 caregivers form the AFTD telephone support group for parents, professionals from the fields of child bereavement, clinical social work/FTD research, family research in dementia and secondary educationSurvey participants (n=24): Age (years): 54.5% between 18 and 25, range 18 to 35Gender: 29.2% male/70.8% femaleAge at disease onset (years): 65.2% age 16 to 18, 21.7% age 13 to 15Diagnosed parent: 56.5 % father, 34.8% mother, 4.2% stepfather, 4.2% stepmother47.6% had been told the name of the parent’s diagnosis, 52.4% had not |
| Methods/measures | Literature review of studies about care in young-onset dementias and children as caregivers, anticipatory griefInternet search of support programs for those childrenAnecdotal data from AFTD telephone support group, in-person support groups and the AFTD HelpLineSurvey of children <18 years of age at onset who live at home with a parent diagnosed with FTD |
| Interventions | n/a |
| Outcomes | Literature findings on dementia caregiving and children and anticipatory grief are presentedThe search for existing programs showed that young-age caregiver support services exist in the United Kingdom, the US and Canada, however special support for children of FTD patients is very limited and mainly contains websites and a one-week summer camp for children or grandchildren of dementia patients regardless of dementia typeOf the 21 respondents, five (23.8%) turned to their well parent when they had questions, another five (23.8%) asked their well parent and the Internet about the condition, four (19%) only used the Internet, five (23.8%) stated they had no-one to turn to or did not want to talk about the condition. Of 19 respondents, six (31.6%) had told their teachers, while 13 (68.4%) had not.18 responses about emotions towards the parent’s diagnosis: “sad”, “angry”, “scared”, and “confused” were most frequentThe well parent and family, especially siblings, were rated most supportiveSports, music, video games, being with friends and away from home were strategies found most helpfulOf 19 respondents, eleven (57.9%) were involved in providing regular or significant care such as companionship and errands – among them five who provided assistance in personal care tasks, e.g. feeding, bathing, toileting-, five (26.3%) did not participate in caregiving, three (15.3%) were unsureBoth positive (e.g. “helpful”, “more grown up”) and negative (“annoyed”, “unfair”) feelings were expressed towards the additional caring responsibilitiesManifestations of the disease that were inconsistent with the parent role or embarrassing were stated most often when asking for difficult aspects; the FTD parent moving into a care home, dealing with the well parent’s emotions and the fear of the well parent becoming sick were also namedThree out of 18 respondents could not find any positive things coming along with the parent’s sickness, some participants stated that they learned to take on more responsibilities, appreciated the family relationship and were more aware of their own lifeThirteen (72.2%) of respondents said they would be interested in meeting other children of FTD patients, 2 (11.1%) were not, 3 (16.7%) were unsure. When asked for the most appealing ways to interact with other relatives of FTD patients, eight (61.5%) listed an in-person event first, followed by phone or support groups; five (38.5%) listed online supports first, followed by group events or support groups for teenagers and childrenChildren of parents participating in the AFTD’s phone support group were given a three-question survey asking for their desire to interact with other children/teenagers about the condition, the most beneficial activities for coping and their most difficult challenges; 12 children from 4 families responded, five (41.7%) wanted to talk to others but did not know how, social networks would not appeal to them; coping activities and challenges were similar to those mentioned in the online survey |
| Limitations | Selection bias via the AFTDMissing answers in the survey |

### 1.1.11 Diehl-Schmid et al. (2013) – Caregiver burden and needs in frontotemporal dementia.

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| Reference | Diehl-Schmid, Janine; Schmidt, Eva-Maria; Nunnemann, Sabine; Riedl, Lina; Kurz, Alexander; Forstl, Hans et al. (2013): Caregiver burden and needs in frontotemporal dementia. In: *Journal of geriatric psychiatry and neurology* 26 (4), S. 221–229. DOI: 10.1177/0891988713498467. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Munich, Germany |
| Aim/subject | To assess specific problems and needs of FTD caregivers as well as factors that contribute to caregiver burden using a standardized questionnaire |
| Participants | 200 questionnaires were sent to caregivers that were recruited from 4 German FTD caregiver support groups, 6 months were assigned for collecting data; a telephone interview with the aim of explaining and clarifying the content of the questionnaire was conducted immediately after the questionnaire was returned to the research center104 caregivers participated, 10 were excluded because patients had already diedDiagnosis of patient: 87% bvFTD, 13% PPA (SD or PNFA) with behavioral symptomsAge of patient: mean 63.94 years (±10.08, range 28-82)Gender of patient: 68% male/32% femaleAge at diagnosis: mean 60.41 years (±9.89, range 22-79)Situation of living: 6% alone, 72% with spouse, 5% with child, 6% with other person, 18% in a nursing homeGerman nursing care level: 32% none, 26% level 1, 22% level 2, 20% level 3Age of caregiver: mean 59.11 years (±11.74, range 24-78)Gender of caregiver: 28% male/72% femaleRelationship to patient: 61% wives, 19% husbands, 12% children (in-law), 8% other (siblings, parents, friends)Time of daily supervision/care for the patient: mean 10.1 hours (±8.8, range 0-24)Time since caregivers knew patients: mean 38.31 years (±13.22, range 10-59)72% living in the same household with the patient, 31% caring for other persons in the household (mainly children), 14 patients had underage (younger than 18 years old) children at the time of first symptoms, 3 patients had underage children at the time of the interview |
| Methods/measures | Development of a standardized questionnaire, including questions about demographic data, disease history, living situation, modes of patient care using Resource Utilization in Dementia lite questionnaire; questions about change in financial situation and change in caregiver-patient relationshipCaregiver strain: assessed using the Caregiver Strain Index (CSI), 13 items that are rated as applying or not, scores of ≥7 indicating a great level of strainCaregiver depression: assessed using the Beck Depression Inventory, second edition (BDI-II), score range 0-63, score 0-8 = no depression, 9-12 = minimal depression, 13-19 = mild depression, 20-28 = moderate depression, ≥29 = severe depressionCaregivers were asked about whether they had received support or interventions; if so, they were asked to rate actual experienced or potential helpfulness of those measures for themselves or other FTD caregivers; 45 support services or interventions were presented, based on experience of the researchers, a worldwide email inquiry about services for FTD caregivers and a review of problems and needs regarding AD caregivers |
| Interventions | None |
| Outcomes | Caregiver depression and strain: 25% had no depression, 27% minimal, 21% mild, 19% moderate, 7% severe, one caregiver did not complete BDI-II;60% had CSI scores ≥7, indicating a great level of strainSymptoms/impairments and their influence on caregiver burden and strain: aggression, lack of manners, occurrence of misdemeanours, inflexibility, egocentric behavior, lack of empathy, addictive behavior, need for supervision, dependency, difficulties swallowing, walking disabilities and incontinence were burdensome for more than 80% of the caregiversDifficult behavioral symptoms and reduced patients’ sleep correlated with higher BDI-II scores, physical impairments correlated with higher CSI scores; apathy and impulsivity seemed to influence CSI scoresOpen question about most burdensome impairment: 45% behavioral symptoms, 25% communication problems, 30% need for careOpen question about worst aspect of the disease (most frequent answers): loss of a loved one, unstoppable disease progression, own helplessnessInfluence of caregiver and patient characteristics on depression and strain: more female caregivers had depression, caregivers of male patients (often their wives) had significant depression, younger patient age at diagnosis and worsening of caregiver-patient relationship were associated with depressionNo differences in depression regarding relationship to patient, living situation, external supportTime of care, number of persons and support services involved in caring, nursing care level did not correlate with depression – however, these factors correlated with CSI scoresCSI scores worse in female and younger caregivers; patients’ age, age at onset and age at diagnosis negatively correlated with caregiver strainDifficult financial situations increased caregiver strain, CSI and BDI-II scores correlated significantlyCaregiver-Patient Relationship: 20% said the disease had improved the relationship, 30% left unchanged, 50% worse relationshipChange in patients’ financial situation: money was tight before onset in the disease in 5% of patients, now it is in 26% of patientsSupport services and interventions: caregivers rated services and interventions regarding the distribution of information the most helpful, followed by psychosocial support through trained personnel and financial support for caregivers; raising awareness for the disease was rated as helpful by almost all caregivers; nonpharmacological treatment for patients and safety measures (e.g. video monitoring) were rated less helpful or importantMeasures rated top 3 most helpful: (1) concrete and thorough explanation of the diagnosis, (2) continued support by a doctor who knows about the disease, (3) to inform and educate doctors about the diseaseAdditional wishes for services: “all-inclusive information packages”, e.g. a contact person who is familiar with legal, financial, social and medical issues concerning FTD instead of various people |
| Limitations | Selection bias from support groupsNo correction for multiple comparisonsJudgment of interventions and support services based on experience and assumptions of caregiversUse of a novel questionnaire instead of pre-existing validated assessment toolsDiagnosis was specified by caregiver report, not objectively confirmedFTD subtypes were not considered separatelyCSI questionable for use in dementia caregivers |

### 1.1.12 Hsieh et al. (2013) – When one loses empathy. Its effect on carers of patients with dementia.

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| Reference | Hsieh, Sharpley; Irish, Muireann; Daveson, Naomi; Hodges, John R.; Piguet, Olivier (2013): When one loses empathy. Its effect on carers of patients with dementia. In: *Journal of geriatric psychiatry and neurology* 26 (3), S. 174–184. DOI: 10.1177/0891988713495448. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Sydney, Australia |
| Aim/subject | To assess loss of empathy in bvFTD, SD, and AD patients and its effect on their caregivers as well as the discrepancy between perceived empathy loss from patients’ and caregivers’ viewpoint |
| Participants | Recruitment from Frontier Frontotemporal Dementia Research group, Sydney; diagnosis confirmed by neurologist according to current diagnostic criteria, patients underwent MRI; healthy controls selected from volunteer panel (Addenbrooke’s Cognitive Examination-Revised score above cutoff 88 of 100)Exclusion criteria: neurological conditions, current psychiatric illness, significant drug or alcohol historyNumber of patient/caregiver dyads: 14 AD, 18 bvFTD, 14 SD, 30 controls (CG)Completion of IRI questionnaire: AD 14 (6 carer only, 8 patient and carer); bvFTD 18 (4 carer only, 14 patient and carer); SD 14 (1 patient only, 5 carer only, 8 patient and carer)Age of patient: AD mean 63.4 years (±7.5), bvFTD mean 63.7 (±7.4), SD mean 64.3 (±8.5), CG mean 68.1 (±5.6)Gender of patient: AD 11 male/3 female, bvFTD 13 male/5 female; SD 9 male/5 female; CG 14 male/16 femaleYears of education: AD mean 13.1 (±3.1), bvFTD mean 11.3 (±2.7), SD mean 13.1 (±3.6), CG mean 13.4 (±2.7)Age of symptom onset: AD mean 59.2 years (±6.3), bvFTD mean 59.9 (±6.9), SD mean 59.9 (±8.7), CG n/aAge of caregiver: not reportedGender of caregiver: AD 3 male/11 female; bvFTD 4 male/14 female; SD 4 male/10 femaleRelationship to patient: AD 12 spouses/2 other; bvFTD 16 spouses/2 other; SD 11 spouses/3 other |
| Methods/measures | Empathy: assessed using the Interpersonal reactivity index (IRI) with four subscales (perspective taking [PT], fantasy [FS], empathic concern [EC], personal distress [PD]), maximum score of subscales = 28, maximum total score = 112, higher scores indicating higher empathy, ratings obtained for time before onset of the disease and present time, not completed by control groups, completed by patients and caregiversCaregiver burden: assessed using the short Zarit Burden Interview (ZBI), maximum score 48, higher scores indicating greater caregiver burdenRelationship quality between caregiver and patient: assessed using the Intimate Bond Measure (IBM) generating care and control scores, maximum score for each of the two is 36Cognitive function of the patient: assessed using the Addenbrooke’s Cognitive Examination-Revised (ACE-R), maximum score 100, higher scores indicating better cognitive functionEmotion recognition: assessed using an emotion selection task developed by the Frontier Frontotemporal Dementia Research Group, participants were asked to identify six basic facial expressions of emotions and a neutral expression in an array of 42 itemsBehavior: assessed using the Cambridge Behavioral Inventory-Revised (CBI-R), maximum score 180, higher scores indicating higher frequency of behavioral problems, completed by caregiverDementia severity: assessed using the Clinical Dementia Rating Scale (CDR), score 0.5 = very mild dementia, 1 = mild, 2 = moderate, 3 = severe; CDR-sum of boxes (CDR-SB) provides finer gradation of impairmentassessed using the Frontotemporal Dementia Rating Scale (FRS), total raw score 30 converted into percentage scores (according to patients’ premorbid routines), final score 5.39 (normal) to -6.66 (profound impairment) |
| Interventions | None |
| Outcomes | Demographic data of carers: equal distribution of caregivers across groups, predominantly spouses and femaleBurden and relationship quality for the carer: ZBI was higher in bvFTD caregivers than in SD; caregivers of bvFTD patients report less caring relationships on the IBM than AD and SD caregivers, SD caregivers describe a significantly more controlling relationship than AD caregiversDemographic Data of Patients and Controls: groups were matched with regard to age, education, sex, age of onset, CDR-SB scoreDisease severity according to FRS was greater in bvFTD compared to SDNeuropsychological and Behavioral Measures of the Patient: all patient groups differed significantly from CG on ACE-R, SD group scored significantly lower than AD and bvFTD group which may be due to the large language component of the testPatient groups performed significantly worse on emotion recognition test, no differences between patient groupsPatient groups matches in CBI-R scoresInterpersonal Reactivity Index – Overall Score: significant diagnosis × rater interaction, interaction for diagnosis and rater separately were not significantOverall change in IRI obtained by caregiver rating was significant with the AD group differing significantly from the bvFTD group, self-rated IRI changes were not significantCarer and patient ratings only differed significantly in the bvFTD groupIRI-Subscale scores – carer ratings: significant diagnosis × subscale interaction, significant main effect for diagnosis, AD group tended to differ from bvFTD group (nonsignificant); significant main effect of subscale with higher levels in personal distress than the other 3 subscales, loss of Empathetic Concern and Perspective Taking significantly different than Fantasy subscalebvFTD group differed significantly from AD group on the Empathetic Concern subscale and the Perspective Taking subscaleIRI-Subscale scores – patient ratings: diagnosis × carer interaction not significant, no main effect for diagnosis, main effect for Subscale was found – higher levels of Personal Distress compared to other 3 subscalesIRI-Subscale scores – differences between caregiver and patient ratings: no differences on the Fantasy subscale, significant differences on the Empathy and Perspective Taking subscales in bvFTD group; significant differences for the Personal Distress subscale in bvFTD and AD groups, trend in SD groupAssociations between Empathy scores and clinical variables: EC and PT scores summed to a total empathy score; significant correlation between empathy loss and lack of a caring relationship in the bvFTD group; trend of correlation between empathy score and perceived burden in SD group; no significant correlations for AD cohortCorrelation between empathy loss and FRS and CBI scores in SD group; correlation between empathy loss and emotion recognition task in AD group, no significant correlation in bvFTD groupNo correlation between empathy scores of patients and carers in any group |
| Limitations | Small sample sizeBefore-onset empathy ratings might be influenced by the current situationEmpathy assessment instrument that dissociates cognitive and emotional components of empathy would be needed in bvFTD patientsLack of information about caregiver characteristics (e.g. age) |

### 1.1.13 Ibach et al. (2004) – Die Situation der Angehörigenberatung bei Patienten mit frontotemporaler lobarer Demenz in der Gerontopsychiatrie.

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| Reference | Ibach, Bernd; Koch, Horst; Koller, Manfred; Hajak, Goran; Putzhammer, Albert (2004): Die Situation der Angehorigenberatung bei Patienten mit frontotemporaler lobarer Demenz in der Gerontopsychiatrie. In: *Psychiatrische Praxis* 31 Suppl 1, S120-2. DOI: 10.1055/s-2004-828467. (ARTICLE IN GERMAN) |
| Type | Epidemiologic study |
| Location/country | Germany |
| Aim/subject | To assess the availability of caregiver counselling specific for FTD in German geriatric psychiatry clinics |
| Participants | Members of the open geriatric psychiatry work group – 36 psychiatric clinics across Germany providing care for an area of >20.000.000 inhabitants, clinically experienced neurologists and psychiatrists |
| Methods/measures | Semi-structured questionnaire with two parts 1) documentation of clinic structure2) record of all patients with a suspected dementia from the FTLD spectrum treated in the clinic in the previous 4 weeksCompleted by neurologists and psychiatrists |
| Interventions | None |
| Outcomes | Disease-specific caregiver counselling provided: 75% of clinicsCaregivers are being referred to local Alzheimer’s societies: 89%Caregivers are being referred to other initiatives: 61%A caregiver support group is offered: 61%There is a general deficiency of support for FTLD patients and their caregivers: 83%Significant negative correlation between size of area a clinic is providing care for and caregiver support offersProportion of patients with dementia showed a significant negative correlation with referrals of caregivers to other institutionsSignificant negative correlation between number of closed ward-beds and disease specific caregiver counsellingCaregiver support groups are mainly directed at Alzheimer’s disease caregiversIncreased size of clinic, as seen in a high number of closed ward-beds, high proportion of patients with dementia and a high number of inhabitants in the area the clinic is providing for seem to complicate caregiver support in clinicsOther data obtained from the questionnaire are discussed in a different article |
| Limitations | Support offers for FTLD caregivers not specifiedNo information about referral to FTLD-specific institutions or FTLD-only caregiver support groups |

### 1.1.14 Kaiser and Panegyres (2006) – The psychosocial impact of young onset dementia on spouses.

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| Reference | Kaiser, Sam; Panegyres, Peter K. (2006): The psychosocial impact of young onset dementia on spouses. In: *American journal of Alzheimer's disease and other dementias* 21 (6), S. 398–402. DOI: 10.1177/1533317506293259. |
| Type | Controlled comparative study |
| Location/country | Australia |
| Aim/subject | To assess psychosocial burden and well-being in spouses of patients with early-onset dementia in Western Australia |
| Participants | Spouses of young-onset dementia patients (onset before 65 years); dementia diagnosis established using Australian National Alzheimer’s Disease Criteria for AD, consensus criteria for FTD and primary progressive aphasia (PPA),120 postal questionnaires sent in June 2004 and responses collated in December 2005, 100 usable responsesAge of caregivers: mean 62.3 years (range 49-73)Gender of caregiver: 46% male/54 % femaleSituation of living: 30% of patients no longer living at home, 25% of caregivers with current employment, 25% of caregivers had completed tertiary education, 10 patients were institutionalized for dementia, 4 patients had diedDiagnosis of patient: 42 patients with FTLD, 36 AD, 6 PPA, 16 miscellaneousMiscellaneous cases contained patients with CADASIL (cerebral autosomal dominant arteriopathy and subcortical infarcts), olivopontocerebellar degeneration, posterior cortical atrophy syndrome, Creutzfeldt-Jakob disease and corticobasal ganglionic degeneration (CBGD) |
| Methods/measures | Two-section postal self-reported questionnaire:1) Caregiver burden: assessed using the Zarit Burden Interview (ZBI), score range 0-88, higher scores indicating greater caregiver burden2) Caregiver depression: assessed using the Beck Depression Inventory (BDI), higher scores indicating higher depression |
| Interventions | None |
| Outcomes | Caregiver burden: no total scores reported for ZBI, top ten most common concerns using cumulative scores from all caregivers given; three most burdensome concerns include 1) feeling that their spouse is dependent on them, 2) feeling afraid of what the future holds for their spouse, 3) feeling stressed between caring for their spouse and trying to meet other responsibilities for their family or workCaregiver depression: 50% of AD caregivers reported at least mild depression compared to 75% of FTLD caregivers; wives reported more (53.4%) depression than husbands (46.6%); highest recorded response was reduced interest in sexSignificant correlation between BDI scores and FTLD diagnosis; no correlation for age of patient, caregiver gender, educational level, employment status, AD or other diagnoses, living situation and BDI scores |
| Limitations | Lack of reported data, e.g. ZBI total scoresNo description of associations between ZBI and BDI scores |

### 1.1.15 Kaizik et al. (2017) – Factors underpinning caregiver burden in frontotemporal dementia differ in spouses and their children.

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| Reference | Kaizik, Cassandra; Caga, Jashelle; Camino, Julieta; O'Connor, Claire M.; McKinnon, Colleen; Oyebode, Jan R. et al. (2017): Factors Underpinning Caregiver Burden in Frontotemporal Dementia Differ in Spouses and their Children. In: *Journal of Alzheimer's disease : JAD* 56 (3), S. 1109–1117. DOI: 10.3233/JAD-160852. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Sydney, Australia |
| Aim/subject | To assess differences in spousal and child caregiver burden, to compare co-resident and live-out child caregiver burden and to examine factors influencing child and spousal caregiver burden |
| Participants | 90 caregivers (47 children, 43 spouses) of FTD patients recruited from Frontier Frontotemporal Dementia Research Group between November 2009 and September 2010, data collected via online survey or from Frontier database71 families involved: 5 families with 2 children, 1 family with 3 children and 11 families with spouse and childPatients’ diagnoses included bvFTD, svPPA, nfvPPA, CBS, PSP, all confirmed according to current criteriaCaregivers in mild to moderate dementia (15 children, 29 spouses):Age of caregiver: children mean 32.2 years (±9.7), spouses mean 62.5 (±10.0)Gender of caregiver: children 87% female, spouses 73% femaleMain carer: children 26%, spouses 89.7%Living in the same house: children 26%, spouses 100%Caregivers in severe to profound dementia (16 children, 10 spouses)Age of caregiver: children mean 30.7 years (±10.1), spouses mean 61.9 (±9.0)Gender of caregiver: children 62.5% female, spouses 71% femaleMain carer: children 18%, spouses 90%Living in the same house: children 18%, spouses 90%Data available for 67/90 participants only due to lack of dementia severity informationComparison of child caregivers:Age of caregiver: same household mean 24.9 years (±5.7), different household mean 35 (±9.4)Gender of caregiver: same household 37.5% female, different household 77% femaleMain carer: same household 12.5%, different household 21% |
| Methods/measures | Caregiver burden: assessed using the short Zarit Burden Interview (ZBI), score range 0-48, scores ≥17 indicating clinically significant burdenCaregiver emotional state: assessed using the short version of the Depression, Anxiety and Stress Scale-21 (DASS 21), scores ≥10 on the depression subscale indicate significant depression, cut-off score on the anxiety subscale ≥8, cut-off score on the stress subscale ≥15Caregiver social network: assessed using the Social Network Index (SNI), assesses participation in 12 types of social relationships Patients’ disease severity: assessed using the Frontotemporal Dementia Rating Scale (FTS-FRS), adjusted scores define six stages of dementia severity - >4.12 = very mild, 4.11 to 1.92 = mild, 1.91 to -0.40 = moderate, -0,39 to -2.58 = severe, -2.59 to -4.99 = very severe, -<4.99 = profoundChange in bond between caregiver and patient: assessed using the Intimate Bond Scale (IBM), subscales control and care, subscale score range 0-36, high care and low control scores indicating a positive relationship |
| Interventions | None |
| Outcomes | 83% of child caregivers did not live in the same house as the person with dementia, 81% of children did not consider themselves as the main caregiverOnly one spousal caregiver did not co-reside since the patient was in full-time residential careCaregiver burden and emotional state: in the mild-moderate dementia group, children and spouses reported of similar levels of burden, depression, anxiety and stress (all below cut-off) In the severe-profound dementia group, children and spouses reported of significant burden, both groups reported of significant depression, anxiety scores were above cut-off for child caregivers only, stress scores were similar and below cut-off in both children and spousesCaregiver social network: child caregivers have significantly less rich social networks than spouses in both mild-moderate and severe-profound dementia groupsBond between patient and caregiver: both dementia severity groups reported of sub-optimal relationships; in mild-moderate dementia patients’ children reported a significantly worse relationship, in severe-profound dementia relationship was significantly worse in spousesChildren in both dementia severity groups reported of a significantly higher controlling relationship from the person with dementiaChildren living with affected parent vs living elsewhere: co-resident children were significantly younger and significantly more likely to be male; living situation did not correlate with main caregiver statusChild caregiver burden, emotional state, and social network: co-residential children reported significantly higher burden than children living in a different household, levels of depression and stress were similar; anxiety levels were similar but with co-residential children scoring above cut-offChild caregivers living at home reported of significantly smaller social networksBond between child caregiver and patient: both groups reported a low level of care from the affected parent but a very controlling relationshipMain factors in caregiver burden: regression analysis with ZBI as dependent variable and caregiver age, DASS 21 depression and anxiety scores, SNI scores, IBM care and control scores and FTD-FRS scores as independent variables; in spouses, dementia severity explained 70% of variance and depression explained 7% of variance in ZBI scores;In children, depression scores accounted for 51% of variance of ZBI scoresYounger age is a high risk for caregiver burden, FTD affects not only the primary caregiver but the whole family; depression and not dementia severity is a main predictor for child caregiver burden |
| Limitations | Not all participants completed the survey fully, some caregivers might not consider themselves the primary carerSocioeconomic differences not measuredNo information about premorbid family situation |

### 1.1.16 Knutson et al. (2008) – Neural correlates of caregiver burden in cortical basal syndrome and frontotemporal dementia.

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| Reference | Knutson, K. M.; Zamboni, G.; Tierney, M. C.; Grafman, J. (2008): Neural correlates of caregiver burden in cortical basal syndrome and frontotemporal dementia. In: *Dementia and geriatric cognitive disorders* 26 (5), S. 467–474. DOI: 10.1159/000167268. |
| Type | Controlled comparative study, descriptive study |
| Location/country | USA |
| Aim/subject | To determine areas of atrophy in patients with FTD and Corticobasal Syndrome (CBS) and their association with caregiver burden |
| Participants | Enrolled at National Institutes of Health after referral, diagnosis confirmed by neurologist and neuropsychologist based on imaging, neurological examination and neuropsychological assessmentExclusion criteria: evidence of head injury, depression, other types of dementia or a condition impairing the ability to complete testing, e.g. inability to speak22 CBS patients, 25 FTD-fv (frontal variant) patients, 14 healthy controls (CG); CBS and FTD-fv patients with their caregiversAge of patients: CBS mean 67.86 years (±8.72), FTD-fv mean 59.84 (±8.33), CG mean 60.57 (±6.35)Gender of patient: CBS 11 male/11 female, FTD-fv 12 male/13 female, CG 7 male/7 femaleMean years of education: CBS 14.41 (±3.05), FTD-fv 14.92 (±3.30), CG 17.14 (±3.46)No caregiver demographic characteristics reported |
| Methods/measures | Caregiver burden: assessed using the Zarit Burden Interview (ZBI), score range 0-88, cut-off score ≥24 indicating caregivers in need of intervention, completed by caregiversDementia severity: assessed using the Mattis Dementia Rating Scale-2 (MDRS-2), lower scores indicating more severe dementia, completed by patients and control groupBehavioral disturbances: assessed using the Neuropsychiatric Inventory (NPI), 10 subscales, higher scores indicating more neuropsychiatric symptoms, completed by caregiversImaging: obtained on a 1.5 Tesla GE scanner (T1-weighted, at least 120 1.5mm axial slices), 1.5 Philips scanner (T1-weighted, 160 1.5mm axial slices) and a 3 Tesla Philips scanner (T1-weighted, 140 1.5mm axial slices) |
| Interventions | None |
| Outcomes | Comparisons between patient groups: CBS group significantly older than FTD-fv group, CG had significantly more years of education than CBS and FTD-fv groups; no significant differences in total intracranial volume (TIV) between any of the three groupsFTD-fv patients showed significantly more neuropsychiatric symptoms as measured by the NPI than CBS patients, with FTD-fv patients having significantly higher scores in every subcategory except for depressionMDRS-2 means did not differ significantly between CBS and FTD-fv patients, scaled scores for FTD-fv indicated severe impairment, CG scored significantly better in MDRS-2; no significant correlations between MDRS-2 and NPI scores, no significant correlation between disease duration and ZBI, NPI or MDRS-2 scoresCaregiver burden: significantly higher burden in FTD-fv caregivers; ZBI scores were mildly correlated with both NPI and MDRS-2 scores in the CBS group, but no significant regression model emergedZBI scores in the FTD-fv group was significantly correlated with NPI but not MDRS-2 scores**,** stepwise multiple regression confirmed that NPI scores explained 16% of ZBI varianceVBM results: both CBS and FTD-fv patient groups showed atrophy especially in the frontal and temporal cortex as compared to the control group; significant association between atrophy in the anterior portion of the left inferior temporal gyrus (ITG) extending to the middle temporal gyrus (MTG) and ZBI scores were found in CBS patients;no significant association found at p < 0.001 for FTD-fv patients, p < 0.005 revealed a correlation between atrophy in the right orbital gyrus and ZBI scores;significant correlation between peak voxel intensity values and MDRS-2 scores for FTD-fv patients only, no significant correlations between NPI scores and peak voxel intensities, analyses of NPI subscales showed significant correlation between apathy and aberrant motor behavior and intensity values at peak voxels in the right orbital gyrus in FTD-fv patientsIn CBS patients, dementia severity leads to higher caregiver burden, in FTD-fv patients increased neuropsychiatric symptoms are associated with caregiver burden |
| Limitations | No specific measures assessing semantic function in CBS patientsNo information about caregiver characteristics (e.g. age, gender) available |

### 1.1.17 Kumfor et al. (2014) – Ecological assessment of emotional enhancement of memory in progressive nonfluent aphasia and Alzheimer’s disease.

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| Reference | Kumfor, Fiona; Hodges, John R.; Piguet, Olivier (2014): Ecological assessment of emotional enhancement of memory in progressive nonfluent aphasia and Alzheimer's disease. In: *Journal of Alzheimer's disease : JAD* 42 (1), S. 201–210. DOI: 10.3233/JAD-140351. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Sydney, Australia |
| Aim/subject | To assess emotional enhancement of memory in patients with progressive non-fluent aphasia (PNFA) in comparison to patients with Alzheimer’s disease (AD) |
| Participants | Recruitment from Frontier Frontotemporal Research Clinic13 PNFA patients, 12 AD patients and 10 healthy age- and education-matched controls (CG), caregivers of AD and PNFA patientsDiagnosis was made according to current consensus criteria, involving a PET scan for 12 of the 13 PNFA patientsExclusion criteria: history of neurological or psychiatric condition including traumatic brain injury or stroke, use of centrally-acting medication, lack of proficiency in English; ≤88/100 score on Addenbrooke’s Cognitive Examination-Revised (ACE-R)Age of patient: PNFA mean 64.5 years (±9.5), AD mean 68.6 (±7.8), CG mean 71.4 (±5.5)Gender of patient: PNFA 5 male/8 female, AD 9 male/3 female, CG 6 male/4 femaleYears of education: PNFA mean 13.2 (±2.8), AD mean11.5 (±3.1), CG mean 14.4 (±3.0)Disease duration in months: PNFA mean 35.8 (±16.1), AD mean 64.0 (±55.2), CG n/aFunctional Rating Scale Rasch Score (higher scores indicating higher functioning): PNFA mean 2.6 (±1.6), AD mean 1.6 (±1.4), CG n/a |
| Methods/measures | Neuropsychological assessment: Functional Rating Scale (FRS) used to measure dementia severity; assessment of attention (Digit Spain Forwards, maximum span; Trail Making Test), assessment of episodic memory (Doors Memory Test, Part A; Rey Complex Figure [RCF] copy and 3-minute delay), assessment of language (naming and comprehension subtests of the Sydney Language Battery), assessment of emotion recognition (Ekman 60)Emotional memory assessment: two versions of a story presented using PowerPoint slides containing three phases with the first and last phase being essentially identical but the middle section containing either an emotional version (i.e. a boy is critically injured in a car accident) or an emotionally neutral version (i.e. a boy passes a minor car accident) – both versions shown in an interval of two weeks; participants were asked to rate the story for understanding and emotionality (/10 each) immediately after presentation, after a 1-hour delay filled with unrelated neuropsychological testing, participants’ episodic memory was tested using a questionnaire of a total of 76 multiple-choice questions referring to the storyCarer burden and wellbeing: assessed using the Zarit Burden Interview (ZBI), assessed using the Depression, Anxiety, and Stress Scale (DASS), both completed by caregivers |
| Interventions | none |
| Outcomes | Demographics and background neuropsychological assessment: PNFA patients performed below controls on a verbal naming task, mild deficits in visuomotor processing speed (Trails A) with intact visuoconstruction ability (RCF copy), impaired facial emotion recognition (Ekman 60);AD patients showed impaired performance on visual recognition task (Doors A) and visual recall memory task (RCF 3-minute delay) in comparison with PNFA and CG, mild impairments in language comprehension with preserved visuoconstruction ability (RCF copy) and emotion recognition (Ekman 60)Emotional memory taskSubjective ratings of understanding and emotionality: no significant difference in ratings of understanding observed between stories or diagnostic groups, Diagnosis × Story version not significant; significant main effect for Story version in ratings of emotionality, no significant main effect for Diagnosis or Diagnosis × Story version, all groups rated the emotional version as significantly more emotional; marginally significant difference in rating of the neutral story with the PNFA group rating it as more emotional than the control groupMemory performance: significant main effect for Diagnosis across story versions and phases with AD patients performing significantly worse on the memory test than PNFA and CG participants; main effect for Story version with the emotional version being remembered better averaged across all groups; emotional and neutral story performances compared for each phase in all groups – the PNFA group remembered a similar amount of details in both story versions across all phases, CG participants remembered significantly more details from phase 2 in the emotional story than in the neutral version with a similar remembrance of phase 1 and 3 content, but performance in phase 2 being significantly higher than in phase 3 of the emotional story, AD patients also remembered significantly more phase 2 details of the emotional version 🡪 controls and AD patients benefitted from emotional context in their memory performance, this effect did not show in PNFA patientsRelationship between emotional enhancement of memory, neuropsychological test performance, and caregiver burden**:** in PNFA patients, memory of the emotional story correlated with better performance in the emotion recognition task and general cognition, no associations between memory of the neutral story and neuropsychological test performance; in AD patients, visual memory recall performance on the RCF positively correlated with memory of the neutral story, no such associations for memory of the emotional story; attention, naming, language comprehension, and an executive function measure did not correlate with performance on the emotional memory task in either groupIn PNFA patients, worse memory on the emotional task were significantly correlated with increased caregiver depression and stress, no association between performance on the neutral story except for a marginally significant correlation with caregiver depression in PNFA; disease severity was not significantly associated with memory for either story version or either group |
| Limitationss | No information about caregiver characteristics (e.g. age, gender) availableSmall sample sizeLack of information about whether language impairments in PNFA patients might influence the emotion recognition task |

### 1.1.18 Kumfor et al. (2016) – Examining the relationship between autobiographical memory impairment and carer burden in dementia syndromes.

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| Reference | Kumfor, Fiona; Teo, Drusilla; Miller, Laurie; Lah, Suncica; Mioshi, Eneida; Hodges, John R. et al. (2016): Examining the Relationship Between Autobiographical Memory Impairment and Carer Burden in Dementia Syndromes. In: *Journal of Alzheimer's disease : JAD* 51 (1), S. 237–248. DOI: 10.3233/JAD-150740. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Sydney, Australia |
| Aim/subject | To assess the relationship of autobiographical memory (ABM) impairment and caregiver burden in Alzheimer’s Disease (AD), semantic dementia (SD) and behavioral-variant frontotemporal dementia (bvFTD) and to establish whether characteristic ABM profiles relate to different forms of caregiver burden |
| Participants | Recruitment from Frontier Frontotemporal Dementia Research Clinic12 AD patients, 10 SD patients, 13 bvFTD patients and their caregivers, 16 healthy age- and education matched controls (CG) recruited from NeuRA volunteer healthy control databaseDiagnosis confirmed according to current consensus criteriaExclusion criteria: current or prior history of psychiatric illness, significant head injury, cerebrovascular disease, alcohol or drug abuse, neurological disorders, lack of proficiency in English, ≤88/100 score on Addenbrooke’s Cognitive Examination-Revised (ACE-R)Age of patient: AD mean 67.4 years (±9.5), SD mean 61.0 (±9.2), bvFTD mean 60.2 (±8.7), CG mean 66.2 (±5.3)Gender of patient: AD 9 male/3 female, SD 8 male/2 female, bvFTD 11 male/2 female, CG 10 male/6 femaleYears of education: AD mean 12.5 (±3.2), SD mean 12.5 (±2.9), bvFTD mean 11.8 (±2.9), CG mean 13.4 (±3.4)Disease duration in months: AD mean 41.4 (±32.9), SD mean 63.0 (±22.5), bvFTD mean 51.7 (±31.7), CG n.a.Frontotemporal dementia Rating Scale (FRS) logit score: AD mean 0.8 (±1.6), SD mean 1.5 (±1.2), bvFTD mean -.07 (±1.4), CG n.a.Caregiver relationship to patient: AD 10 spouses/1 child/1 friend; SD 8 spouses/1 child/1 sibling; bvFTD 9 spouses/2 children/2 siblingsGender of caregiver: 30 (86.7%) female |
| Methods/measures | Background neuropsychological assessmentGeneral cognition: assessed using the ACE-R; Attention and memory: assessed using the Digit Span and Trail Making Test; Verbal episodic memory: assessed using the delayed recall subscale of the Rey Auditory Verbal Learning Test (RAVLT, not administered to SD patients due to language deficits); non-verbal episodic memory and visuospatial construction: assessed using the Rey Complex Figure (RCF); naming, comprehension, repetition and non-verbal semantic matching: assessed using the Sydney Language Battery (SYDBAT)Autobiographical memory assessment: structured Autobiographical Interview (AI) was employed to assess autobiographical episodic and semantic information; participants were asked to describe personally experienced events in four time periods (teenage years, early adulthood, middle adulthood and recent time, i.e. within the past 12 months; the original fifth episode from childhood was not employed in this version) without prompting – the Free Recall section; the General Probing section follows (generic cues focusing on a specific event if this had not been achieved previously), then followed by the Specific Probing section (specific questions covering event, time, place, perceptual and emotion of an event), events must be one-off occurrences, limited in time (i.e. a few hours) and specific to a particular locationInterviews were recorded and transcribed for scoring, scoring based on number of details generated during the interview, divided into details internal and external to the event, focus on internal details – two scores: Total Remote Recall (number of details following general and specific probing in teenage years, early and middle adulthood events) and Total Recent RecallBehavioral symptoms and functional impairment: assessed using the Cambridge Behavioral Inventory-Revised, total score being the average frequency of behaviors, subdomain scores also providedassessed using the Frontotemporal dementia Rating Scale (FRS) to describe disease severity, logit score >4.12 = very mild, 4.11 to 1.92 = mild, 1.91 to -0.40 = moderate, -0.39 to -2.58 = severe, -2.57 to -4.99 = very severe -<4.99 = profoundCaregiver burden and wellbeing: assessed using the short Zarit Burden Interview (ZBI), cut-off score ≥12 indicating high burdenassessed using the Depression, Anxiety, and Stress Scale (DASS), calculating a total score of the three subscales for analysesassessed using the Intimate Bond Measure (IBM) to determine care and control subscales from the patient towards the caregiver |
| Interventions | None |
| Outcomes | Demographics and cognition: bvFTD patients had significantly higher functional impairment than SD patients but no difference between bvFTD and AD group; all patient groups performed worse than CG on the ACE-R with the SD group performing significantly worse than bvFTD and AD groups due to the language impairments; SD patients showed significant language impairments except for Repetition with preserved attention, working memory and visuospatial ability; bvFTD patients showed impairments in working memory and attention, they performed worse on all memory tasks but with preserved visuospatial abilitiesAutobiographical Interview Performance: Significant main effect for Diagnosis with bvFTD and AD patients performing worse than CG in both time periods and SD patients not differing significantly from CG in overall ABM retrieval, no significant differences between patient groups; Significant main effect for Time with more details remembered in all patient groups in Recent time period compared to Remote; main effect for Time × Diagnosis approached significance leading to analyses for each diagnostic group for each time period;SD patients tended to be impaired in Remote time period while Recent time period ABM was relatively intact with a significant difference in performance between Remote and Recent ABM; bvFTD patients performed worse than CG in both time periods with no significant difference in performance between Remote and Recent within the group, i.e. a generally impaired ABM retrieval showedCaregiver burden and well-being: equally high levels of burden in all patient groups; equally high levels of DASS scores;Level of caring relationship (IBM) significantly higher in AD compared to bvFTD, degree of Control was significantly greater in SD compared to AD but similar compared to bvFTDCorrelational analyses: in AD, reduced Recent ABM was associated with worse DASS scores; in SD, reduced Remote ABM was associated with higher Control IBM scores; in bvFTD, no significant correlation was found In AD, behavior change (CBI) was associated with increased ZBI scores and worse DASS scores; in SD, higher CBI scores were related to higher ZBI scores, lower IBM Care scores and worse DASS scores, worse FRS scores were related to high ZBI scores;In bvFTD worse FRS scores were related to lower IBM Care scoresbvFTD caregivers may be more aware of behavioral changes than SD caregivers and therefore CBI scores do not influence bvFTD caregiver burden to the same extent |
| Limitations | Small sample sizeMultiple complex assessments for patientsLack of information about caregiver characteristics (e.g. age) |

### 1.1.19 Lima-Silva et al. (2015) – Neuropsychiatric symptoms, caregiver burden and distress in behavioral-variant frontotemporal dementia and Alzheimer’s disease.

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| Reference | Lima-Silva, Thais Bento; Bahia, Valeria Santoro; Carvalho, Viviane Amaral; Guimaraes, Henrique Cerqueira; Caramelli, Paulo; Balthazar, Marcio Luiz et al. (2015): Neuropsychiatric Symptoms, Caregiver Burden and Distress in Behavioral-Variant Frontotemporal Dementia and Alzheimer's Disease. In: *Dementia and geriatric cognitive disorders* 40 (5-6), S. 268–275. DOI: 10.1159/000437351. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Brazil |
| Aim/subject | To assess the impact of behavioral, functional and cognitive impairment in bvFTD and AD patients on caregiver burden and to compare burden and distress between both dementia types |
| Participants | 50 patients (20 bvFTD, 30 AD) were invited to participate in the study, diagnosis made by neurologist or psychiatrist according to DSM-IV dementia criteria and Neary criteria for bvFTD or NINCDS-ADRDA criteria for AD, respectivelyInclusion criteria: age ≥55 years, at least 2 years of formal education, primary caregiver (3 AD caregivers were formal caregivers)Exclusion criteria: age <55 years; Clinical Dementia Rating >1; visual, hearing or motor impairments that could influence execution of cognitive tasks; uncontrolled chronic conditions such as hypertension or diabetes; psychiatric or neurological disorders, dementia other than AD or bvFTDAge of patient: bvFTD mean 67.05 years (±6.61), AD mean 68.70 (±6.80)Gender of patient: bvFTD 30% female, AD 43.33% femaleYears of schooling: bvFTD mean 9.55 (±5.91), AD mean 8.63 (±4.54)Age of caregiver: bvFTD mean 56.90 years (±15.33), AD mean 50.93 (±14.01)Gender of caregiver: bvFTD 85% female, AD 80% femaleYears of schooling: bvFTD mean 10.05 (±4.54), AD mean 9.63 (±4.06)Relationship to patient; bvFTD 65% spouses/20% daughters, AD 30% spouses/26.66% daughters |
| Methods/measures | Patients’ cognitive status: assessed using the Addenbrooke’s Cognitive Examination-Revised (ACE-R), assessed using the Executive Interview with 25 items (EXIT-25), administered to patientsPatients’ functional performance: assessed using the Direct Assessment of Functional Status – Brazilian Version (DAFS-BR), administered to patients; assessed using the Disability Assessment for Dementia (DAD), administered to caregiversPatients’ anxiety and depression: assessed using the Geriatric Anxiety Inventory (GAI), administered to patients, assessed using the Cornell Scale for Depression in Dementia (CSDD), administered to caregiversCaregiver burden and distress: assessed using the short Zarit Burden Interview (ZBI), assessed using the Neuropsychiatric Inventory-Distress (NPI-D) subscale, administered to caregiversPatients’ behavioral symptoms: assessed using the short NPI, administered to caregivers |
| Interventions | None |
| Outcomes | AD patients scored worse on MMSE and DAFS-BR compared to bvFTD while bvFTD patients were more impaired on the DADNPI subdomain scores were significantly higher for bvFTD patients Caregiver groups were matched in age, gender and education; NPI-D scores were significantly higher in bvFTD caregivers while ZBI scores were similarMost distressing symptoms reported in bvFTD patients were apathy, disinhibition (both being significantly higher than in AD), irritability and agitation/aggression; most distressing symptoms in AD patients were depression and anxiety In bvFTD caregivers, the NPI-D score was associated with EXIT-25 and DAFS-BR scores; in AD caregivers, the NPI-D score was associated with CSDD scoresIn bvFTD caregivers, ZBI scores were associated with ACE-R, EXIT-25 and DAFS-BR scores; no such correlations were found in AD caregiver burdenNo significant difference in burden between AD and bvFTD caregivers found – AD caregivers tended to report higher burden |
| Limitations | Three caregivers were not informal in AD patient groupSmall sample sizeAge restriction (might not include younger onset cases)Use of MMSE in FTD patients questionable (Piguet et al. 2013) |

### 1.1.20 Liu et al. (2017) – The effects of behavioral and psychological symptoms on caregiver burden in frontotemporal dementia, Lewy body dementia, and Alzheimer’s disease. Clinical experience in China.

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| Reference | Liu, Shuling; Jin, Yi; Shi, Zhihong; Huo, Ya Ruth; Guan, Yalin; Liu, Mengyuan et al. (2017): The effects of behavioral and psychological symptoms on caregiver burden in frontotemporal dementia, Lewy body dementia, and Alzheimer's disease. Clinical experience in China. In: *Aging & mental health* 21 (6), S. 651–657. DOI: 10.1080/13607863.2016.1146871. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Tianjin, China |
| Aim/subject | To assess which behavioral and psychological symptoms (BPSD) influence caregiver burden in FTD, AD and Lewy Body Dementia (DLB), to compare burden between those dementia forms and to establish caregiver and patient variables that contribute to caregiver burden |
| Participants | Patients in Tianjin memory clinic recruited between June 2014 and July 2015, diagnosis confirmed there according to Neary criteria for FTD and NINCDS-ADRDA criteria for AD, exclusion criteria: irregular visits at the memory clinic, caregiver interacting less than 8h/dDiagnosis of patient: bvFTD 51, nfvPPA 15, svPPA 16, DLB 22, AD 110Age of patient (mean years): bvFTD 68.94 (±8.11), nfvPPA 67.80 (±8.58), svPPA 67.12 (±9.39), DLB 74.23 (±7.99), AD 70.51 (±9.96)Age of onset (mean years): bvFTD 64.86 (±7.80), nfvPPA 63.60 (±7.72), svPPA 62.12 (±9.01), DLB 72.18 (±7.88), AD 69.84 (±8.43)Gender of patient: bvFTD 60.8% female, nfvPPA 60.0% female, svPPA 68.8% female, DLB 45.5% female, AD 52.7% femaleDisease duration (mean years): bvFTD 4.31 (±1.53), nfvPPA 4.20 (±2.78), svPPA 5.00 (±1.89), DLB 4.32 (±2.03), AD 4.53 (±1.41)Age of caregiver (mean years): bvFTD 55.08 (±13.18), nfvPPA 60.20 (±16.84), svPPA 62.75 (±14.39), DLB 60.18 (±10.79), AD 61.03 (±14.71)Gender of caregiver: bvFTD 43.1% female, nfvPPA 40.0% female, svPPA 25.0% female, DLB 68.2% female, AD 59.1% femaleHours of caregiving/day: bvFTD 12.57 (±9.01), nfvPPA 16.20 (±9.98), svPPA 16.38 (±9.19), DLB 13.14 (±9.16), AD 12.40 (±8.74)Relationship to patient: bvFTD 27 spouses, 22 children, 2 other; nfvPPA 11 spouses, 4 children; svPPA 12 spouses, 4 children; DLB 11 spouses, 11 children; AD 62 spouses, 41 children, 7 other |
| Methods/measures | Cognitive functioning: assessed using the Mini Mental State Examination (MMSE), score range 0-30; assessed using the Montreal Cognitive Assessment (MoCA), score range 0-30, can detect mild cognitive impairment; assessed using the Clock Drawing Test (CDT), score range 0-4; lower scores on all assessments indicate worse cognitive functioningDementia severity: assessed using the Clinical Dementia Rating Scale (CDR)BPSD: assessed using the Chinese version of the Neuropsychiatric Inventory (NPI), score range 0-144, higher scores indicating higher behavioral impairmentOther patient variables: Activities of Daily Living (ADL)Caregiver burden: assessed using the Zarit Burden Interview (ZBI)Other caregiver variables: relationship, years of care, hours of daily care, income (yuan/month) |
| Interventions | None |
| Outcomes | More than half of FTD group caregivers were male (in contrast to AD and DLB caregivers)bvFTD caregivers had significantly higher burden Patient age and age of onset was lower in FTD group than in AD and DBL groupsADL scores were lower and NPI scores higher in FTD variants than in AD and DBLAberrant motor behavior was the symptom most frequently related to caregiver burden in FTD in general and in bvFTD, no such correlation for nfvPPA and svPPA subgroup analysesPredictors for caregiver burden in FTD were total NPI scores, agitation and aberrant motor behaviorNPI total scores predicted burden in the bvFTD groupMost frequently observed symptoms in FTD: agitation, disinhibition, irritability Most frequent symptoms did not correlate strongest with caregiver burden |
| Limitations | Small sample size especially of nfvPPA and svPPA groupsOnly full-time caregivers were consideredOlder diagnostic criteria were used in bvFTD and aphasia Use of MMSE in FTD patients questionable (Piguet et al. 2013) |

### 1.1.21 Mekala et al. (2013) – Cultural differences are reflected in variables associated with carer burden in FTD. A comparison study between India and Australia.

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| Reference | Mekala, Shailaja; Alladi, Suvarna; Chandrasekar, Kammammettu; Fathima, Safiya; M.O.'Connor, Claire; McKinnon, Colleen et al. (2013): Cultural differences are reflected in variables associated with carer burden in FTD. A comparison study between India and Australia. In: *Dement. neuropsychol.* 7 (1), S. 104–109. DOI: 10.1590/S1980-57642013DN70100016. |
| Type | Controlled comparative study, descriptive study |
| Location/country | India, Australia |
| Aim/subject | To compare caregiver burden, stress, depression and anxiety of FTD caregivers between India and Australia and to assess which variables are associated with caregiver burden. |
| Participants | 69 caregiver dyads (=138 participants), 31 from India/38 from AustraliaRecruitment from India at the Nizam’s Institute of Medical Sciences Memory Clinic in Hyderabad between December 2009 and May 2012, from Australia in Frontier FTD research group in Sydney between December 2007 and May 2011Inclusion criteria: FTD diagnosis according to consensus criteria, exclusion criteria: major depressive illness in patients, caregivers who are not relatives of the patientAge of caregiver (years): India mean 54.7 (±11.1), Australia mean 57.7 (±13.2)Gender of caregiver: India 61.3% females, Australia 78.9% femalesEducation (years): India mean 13.6 (±4.2), Australia mean 13.3 (±2.9)Number of people helping the caregiver regularly: India mean 1.9 (±0.8), Australia mean 1.5 (±0.7)Hours of weekly care: India mean 101.4 (±66.3), Australia mean 64.2 (±57.5)Length of symptoms (years): India mean 2.6 (±1.9), Australia mean 3.3 (±1.9)Disease severity (FRS score): India mean -1.418 (severe), Australia 0.035 (moderate)Living situation: India - all 31 patients living in the community, Australia - 37/38 patients living in the community |
| Methods/measures | Caregiver burden: assessed using the short Zarit Burden Interview (ZBI), maximum score 48, scores ≥17 indicating significant burden, self-completedCaregiver depression, anxiety, and stress: assessed using the Depression, Anxiety and Stress Scale 21 (DASS 21), maximum score 42; depression cut-off ≥10, anxiety cut-off ≥8, stress cut-off ≥15, self-completedDementia severity: assessed using the Frontotemporal Dementia Rating Scale (FTD-FRS), six severity stages, scores adjusted for pre-morbid functioning, administered by research staff |
| Interventions | None |
| Outcomes | Dementia severity and hours of weekly care were significantly higher in IndiaCaregiver burden was not significantly different in both countries; in India, 61.3% of carers reported high burden levels, in Australia, 55.3% didNo significant differences were found in depression and stress scores. Indian caregivers reported significantly higher levels of anxiety. Significant anxiety was most common in India with 35.5% vs. 20% in Australia. Depression was most common in Australia with 36% vs. 29% in India. High levels of stress were reported by 22.6% in India and 9.1% in Australia.In correlation analyses, caregiver burden was not associated with dementia severity in Indian caregivers, but significantly associated with depression, anxiety, and stress. In Australia, caregiver burden was significantly associated with stress and depression, but not dementia severity. |
| Limitations | Small sample sizes in both countriesNo comparison of support servicesSome measures were newly introduced in India, no information about applicability of assessment for Indian cohortsNo differentiation of FTD subtypes |

### 1.1.22 Merrilees et al. (2010) – Gender differences in the experience of dementia family caregivers.

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| Reference | Merrilees, Jennifer; Wong, Cindy C.; Ketelle, Robin; Wallhagen, Margaret; Miller, Bruce L. (2010): Gender differences in the experience of dementia family caregivers. In: *Alzheimer's & Dementia* 6 (4), S336. DOI: 10.1016/j.jalz.2010.05.1125. |
| Type | Controlled cohort study, descriptive study (poster presentation) |
| Location/country | USA |
| Aim/subject | To examine gender differences in caregiving for early-onset AD patients and FTD patients |
| Participants | Recruitment of primary caregivers in an NIH-funded FTD project, sub-project “The Experience of Family Caregiving”Gender of caregiver: 22 male/42 femaleLiving situation: 84.4% spouses, 89.1% married, 87.5% living with the patient, 98.4% knew the patient for more than 10 yearsDiagnosis of patient: 28 AD (43.8%), 36 FTD (56.3%) |
| Methods/measures | Caregiver burden: assessed using the Caregiver Strain Index (CSI)Caregiver depression: assessed using the Beck Depression Inventory (BDI)Control: assessed using the Perceived Control Questionnaire (PCQ-15)Health-related QoL: assessed using the SF-36 |
| Interventions | None |
| Outcomes | Levels of Strain and Depression were higher among female caregiversMale caregivers had higher PCQ-15 scores, indicating a higher sense of control62% of caregivers rated their health the same as in the previous yearMale caregivers had a better perceived health on the SF-36 than females |
| Limitations | Lack of reported dataNo specification whether findings reached significanceCSI questionable for use in dementia caregivers |

### 1.1.23 Miller et al. (2013) – Identifying cognitive and demographic variables that contribute to carer burden in dementia.

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| Reference | Miller, Laurie A.; Mioshi, Eneida; Savage, Sharon; Lah, Suncica; Hodges, John R.; Piguet, Olivier (2013): Identifying cognitive and demographic variables that contribute to carer burden in dementia. In: *Dementia and geriatric cognitive disorders* 36 (1-2), S. 43–49. DOI: 10.1159/000347146. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Sydney, Australia |
| Aim/subject | To examine the impact of caregivers’ and patients’ demographics, patients’ cognitive impairment and dementia diagnosis on caregiver burden |
| Participants | Recruited from Frontier FTD Research Clinic, diagnosis confirmed according to current criteria, caregiver information obtained within 6 months of clinical and cognitive assessments, exclusion of patients with non-progressive (phenocopy) type FTLDDiagnosis of patient: 35 Alzheimer pathology (23 AD, 12 logopenic progressive aphasia), 61 FTLD (26 bvFTD, 16 SD, 8 PNFA, 11 CBS)Age of patient: AD mean 66.1 years (±8.5), FTLD mean 63.1 (±8.8)Gender of patient: AD 63% male, FTLD 71% maleDisease duration in years: AD mean 3.6 (±2.9), FTLD mean 4.1 (±2.4)Age of caregiver: AD mean 61.9 years (±10.7), FTLD mean 59.4 (±11.4)Gender of caregiver: AD 26% male, FTLD 26% maleRelationship to patient: AD 83% spouses, FTLD 82% spouses  |
| Methods/measures | Caregiver burden: assessed using the short Zarit Burden Interview (ZBI), score range 0-48, cut-off score ≥17 used for indication of significantly high burdenPatient’s general cognition: assessed using Addenbrooke’s Cognitive Examination-Revised (ACE-R)Memory: assessed using Doors A subtest (from the Doors and People memory test) to measure anterograde memory, number of correctly memorized doors from a set of 12 converted into an age-scaled scoreWord Generation and Impulse Control: assessed using the Hayling test, patients have to finish 15 sentences with a word that fits in the first part (Hayling Score A) and an unrelated word in the second part (Hayling score C), both scores age-adjusted, not completed by all participants due to language impairmentsEmotion Recognition: assessed using the Facial Affect Selection test (FAST)Higher scores indicated better function in all tests administered to patients |
| Interventions | None |
| Outcomes | FTLD patients scored significantly worse on Hayling C, i.e. making more impulse control errorsCaregiver burden was significantly higher in FTLD caregiversA younger age (caregivers and patients), a diagnosis of FTLD, lower cognitive scores (emotion recognition, memory, impulse control) contributed to caregiver burdenMultivariate regression model contained patient age, FAST score and Doors and People A score as predictors, explaining 23% of variance in ZBI scores, all scores independently contributed significantly to the model |
| Limitations | Impulse control test could not be administered to severely language-impaired patientsFTD subtypes were not considered separately in analyses |

### 1.1.24 Mioshi et al. (2009) – Factors underlying caregiver stress in frontotemporal dementia and Alzheimer’s disease.

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| Reference | Mioshi, Eneida; Bristow, Matt; Cook, Rachel; Hodges, John R. (2009): Factors underlying caregiver stress in frontotemporal dementia and Alzheimer's disease. In: *Dementia and geriatric cognitive disorders* 27 (1), S. 76–81. DOI: 10.1159/000193626. |
| Type | Controlled cohort study, descriptive study |
| Location/country | United Kingdom |
| Aim/subject | To assess the factors that contribute to caregiver stress in FTD and AD |
| Participants | Patients (diagnosed by a behavioral neurologist) and caregivers recruited via Pick’s Disease Association UK and Alzheimer’s Association UK, completed postal surveysDiagnosis of patient: 34 FTD living in nursing homes (FTDNH), 45 FTD community dwellers (FTDCD), 29 AD community dwellers (ADCD)Age of patient (years): FTDNH mean 66.8 (±7), FTDCD mean 68.8 (±8.7), ADCD mean 70.4 (±7.9)Length of symptoms (unit of time not stated): FTDNH mean 10.2 (±4.5), FTDCD mean 8.3 (±4.2), ADCD mean 7 (±4.3)Age of caregiver (years): FTDNH mean 62 (±10.5), FTDCD mean 63.5 (±10.2), ADCD mean 69.9 (±7.1)Gender of caregiver: FTDNH 82% female, FTDCD 76% female, ADCD 69% female |
| Methods/measures | Patient’s behavior change: assessed using the Neuropsychiatric Inventory Questionnaire (NPI-Q), score range of number of symptoms 0-12, score range of symptom severity: 0-36Patient’s activity of daily living: assessed using a modified version of the Disability Assessment of Dementia (DAD), sub-scores for basic activities of daily living (BADLs) and instrumental activities of daily living (IADLs), adjusted for patient’s premorbid activities, scores converted into percentagesCaregiver stress: assessed using the Perceived Stress Scale (PSS), cut-off calculated as 22.1Caregiver depression: assessed using the Center for Epidemiological Studies Depression Scale (CES-D), score range 0-60, cut-off ≥16Caregiver’s social network: assessed using the Social Network Index (SNI), focusing on the number of high-contact roles |
| Interventions | None |
| Outcomes | Caregiver age significantly higher in ADCD caregiversFTDNH patients were significantly more impaired on BADLs and IADLs FTDCD patients scored significantly higher in NPI symptom severity score and also showed a trend to having more symptoms than FTDNH patientsCommunity dwelling patients were equally impaired on BADLs (moderate to severe) and IADLs (severe) FTDCD patients had a significantly higher number of symptoms on the NPI than ADCD patients, but severity was similarLevels of stress and depression were similar in both FTDNH and FTDCD caregiversFTDNH caregivers had a significantly higher number of social contacts on the SNI than FTDCD caregiversFTDCD caregivers had significantly higher stress and a higher percentage of caregivers with high stress than ADCD caregivers, even after controlling for age and disease durationThe level of depression of FTDCD was twice as high as that of ADCD caregivers, female caregivers reported higher levels of stress and depression in both CD caregiver groupsThere were no differences in the social network of FTDCD and ACDC caregivers.Level of depression (CES-D) scores explained 58.2% of variance in stress scores of FTD caregivers.  |
| Limitations | Small sample sizeNo ADNH group |

### 1.1.25 Mioshi et al. (2013) – The impact of dementia severity on caregiver burden in frontotemporal dementia and Alzheimer’s disease.

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| Reference | Mioshi, Eneida; Foxe, David; Leslie, Felicity; Savage, Sharon; Hsieh, Sharpley; Miller, Laurie et al. (2013): The impact of dementia severity on caregiver burden in frontotemporal dementia and Alzheimer disease. In: *Alzheimer disease and associated disorders* 27 (1), S. 68–73. DOI: 10.1097/WAD.0b013e318247a0bc. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Sydney, Australia |
| Aim/subject | To assess the impact of disease severity and patient and caregiver variables on caregiver burden in FTLD subtypes and AD |
| Participants | Caregivers recruited from Frontier FTD Research Clinic in Sydney; patient diagnoses made according to consensus criteriaDiagnosis of patient: 17 bvFTD, 20 SD, 20 PNFA, 19 ADAge of patient (years): bvFTD mean 59 (±10.6), SD mean 64.8 (±7.8), PNFA 68.1 (±9.8), AD 67 (±9)Gender of patient: bvFTD 70.6% male, SD 60% male, PNFA 65% male, AD 73.7% maleLength of symptoms (years): bvFTD mean 3.3 (±2.6), SD mean 4.3 (±2), PNFA mean 3.1 (±1.7), AD mean 2.9 (±2.2)Age of caregiver (years): bvFTD mean 57.3 (±11.9), SD mean 55.7 (±13.4), PNFA mean 64.6 (±11.3), AD mean 61.1 (±13.4)Gender of caregiver: bvFTD 76% female, SD 70% female, PNFA 75% female, AD 79% femaleRelationship to patient: bvFTD 77% spouses, SD 65% spouses, PNFA 85% spouses, AD 90% spouses  |
| Methods/measures | Caregiver burden: assessed using the short Zarit Burden Interview (ZBI), cut-off score for significant burden ≥17Caregiver depression and anxiety: assessed using the Depression, Anxiety and Stress Scale 21 (DASS 21), cut-off for depression subscale ≥10, for anxiety ≥8, for stress ≥15Caregiver social network: assessed using the Social Network Index (SNI), focusing on number of high-contact rolesQuality of bond between caregiver and patient: assessed using the Intimate Bond Measure (IBM), two subscales of Care and Control from the patient towards the caregiverPatient’s general cognition: assessed using the Addenbrooke’s Cognitive Examination-Revised (ACE-R), maximum score 100, higher scores indicating better cognitive functionDisease severity: assessed using the Frontotemporal Dementia Rating Scale (FRS), 6 stages of severity. 5.39 to 4.12 = very mild, 3.35 to 1.92 = mild, 1.68 to -0.40 = moderate, -0.59 to -2.58 = severe, -3.09 to -4.99 = very severe, -4.98 to -6.66 = profound, obtained through caregiver interviewPatient’s behavioral change: assessed using the Cambridge Behavioral Inventory-Revised (CBI-R), focusing on the domains of abnormal behavior, stereotypic and motor behaviors, and apathy, scores converted into percentages |
| Interventions | None |
| Outcomes | PNFA patients significantly older than bvFTD patients, mostly female caregiversbvFTD caregivers had significantly higher burden than other diagnostic groups, only 25% of PNFA caregivers reported burdenbvFTD caregivers reported significantly higher depressive symptoms, no differences in anxiety and stress scores between groupsNo significant differences in social contacts across groupsbvFTD patient-caregiver dyads scored significantly lower on the IBM care score than all other diagnostic groups; in the SD group, the control scores were significantly higher than in the AD groupSD patients were significantly more impaired on the ACE-R than bvFTD and AD patientsbvFTD patients had significantly more severe dementia than all other groupsBehavioral changes present across all groups, especially in bvFTD and SD groups, but with SD not differing significantly from AD and PNFA groups59% of variance in ZBI scores were explained by disease severity, caring relationship, and caregiver depression. FRS scores alone accounted for 48% of ZBI variance.Caregiver burden increases with disease progression, but other factors, e.g. relationship and depression, contribute to it as well. |
| Limitations | Small sample size |

### 1.1.26 Mourik et al. (2004) – Frontotemporal dementia. Behavioral symptoms and caregiver distress.

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| Reference | Mourik, J. C.; Rosso, S. M.; Niermeijer, M. F.; Duivenvoorden, H. J.; van Swieten, J. C.; Tibben, A. (2004): Frontotemporal dementia. Behavioral symptoms and caregiver distress. In: *Dementia and geriatric cognitive disorders* 18 (3-4), S. 299–306. DOI: 10.1159/000080123. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Netherlands |
| Aim/subject | To determine clusters of behavioral problems and their impact on caregiver burden in FTD |
| Participants | Recruitment via yearly postal and telephone enquiries between January 1994 and June 2002 in nationwide outpatient clinics, data from FTD caregivers (diagnosis confirmed according to Lund-Manchester Criteria), usable results of 63 participants (response rate 72.4%)Age of patient (years): mean 60.7 (±9.6)Gender of patient: 24 male/39 femaleLiving situation: 29 at home/34 in a nursing homeDisease duration (years): mean 6.7 (±3.3)Age of caregiver (years): mean 57.1 (±11.6)Gender of caregiver: 29 male/34 femaleRelationship to patient: 51 spouses/9 children/3 other |
| Methods/measures | Psychopathology: assessed using the Neuropsychiatric Inventory (NPI), subdomain score range 1-12, total score maximum 120, total distress score maximum 50, Dutch versionFunctional and cognitive decline: assessed using the Global Deterioration Scale (GDS), dementia severity stages 1-7 (most severe impairment) |
| Interventions | none |
| Outcomes | Behavioral cluster A comprised delusions, hallucinations, irritability and agitation; cluster B comprised depression and anxiety, other symptoms included euphoria, disinhibition, aberrant motor behavior and apathyEven though patients living at home did exhibit more behavioral symptoms, there was no difference on the overall NPI score, indicating that symptoms of patients in nursing homes are rated as more frequent and more severe.Depression in patients is accompanied by a high level of distress in caregivers.NPI total scores and NPI distress scores were strongly related.Most NPI domains were associated with a medium level of distress, delusions and depression evoking a high level of distress.Caregivers of patients living at home scored significantly higher on the NPI-D than those of patients in nursing homes; GDS scores were significantly correlated to caregiver stress; female caregiver gender was significantly, but not strongly, related to distressCluster A seemed to explain the highest proportion of variance in NPI-D scores as determined by a regression analysis, followed by cluster B and aberrant motor behavior; the predictive values of these domains seemed to be higher than that of the NPI total score |
| Limitations | No differentiation of FTD subtypes |

### 1.1.27 Nicolaou et al. (2010) – Identifying needs, burden, and distress of carers of people with frontotemporal dementia compared to Alzheimer’s disease.

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| Reference | Nicolaou, Paula L.; Egan, Sarah J.; Gasson, Natalie; Kane, Robert T. (2010): Identifying needs, burden, and distress of carers of people with Frontotemporal dementia compared to Alzheimer’s disease. In: *Dementia (London, England)* 9 (2), S. 215–235. DOI: 10.1177/1471301209354024. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Australia |
| Aim/subject | To compare burden, needs, depression and anxiety in FTD caregivers with AD caregivers.  |
| Participants | Recruitment from Alzheimer’s Australia WA, Ltd. and healthcare professional referrals; n=30 FTD patients and n=30 AD patients with their caregivers, verified specialist’s diagnosisAge of patient (years): FTD median 64 (IQR 13), AD median 76.5 (IQR 10)Gender of patient: FTD 90% male/10% female, AD 47% male/53% femaleLength of diagnosis (months): FTD mean 45.4 (±24.5), AD mean 38.8 (±23.3)Living arrangement: FTD 100% supported, AD 7% independent/93% supportedLiving environment: FTD 73% community/27% residential care, AD 83% community/17% residential careAge of caregiver (years): FTD median 58.5 (IQR 13), AD median 67 (IQR 23)Gender of caregiver: FTD 7% male/93% female, AD 30% male/70% femaleRelationship to the patient: FTD 94% partner/6% child, AD 70% partner/30% childLiving situation: FTD 93% with patient/7% without patient, AD 77% with patient/23% without patientLength of time caring (years): FTD mean 5.6 (±2.4), AD mean 5.1 (±3.1)Hours of weekly care: FTD mean 2.7 (±0.6), AD mean 2.5 (±0.7)Financial situation: FTD 40% satisfied/60% not satisfied, AD 67% satisfied/33% not satisfied  |
| Methods/measures | Caregivers underwent a two-hour semi-structured interview (without the patient) followed by the completion of subsequent assessment toolsPatient behavior: assessed using the Revised Memory and Behavior Problems Checklist (RMBPC), score range 0-96, higher scores indicating greater behavioral disturbance and greater impact on caregiversCaregiver needs and received help: assessed using the Camberwell Assessment of Need for the Elderly (CANE), patient- and carer-related areas are assessed for needs, help received for those needs and whether help is satisfactoryCaregiver burden: assessed using the Zarit Burden Interview (ZBI), score range 0-88, scores 21-40 = little burden, 41-60 = moderate burden, >60 = severe burdenCaregiver depression, anxiety, and stress: assessed using the Depression, Anxiety and Stress Scale (DASS 21), score range 0-63, higher total scores indicating greater levels of distress |
| Interventions | None |
| Outcomes | Caregiver needs: female gender was significantly correlated with greater overall needs as a caregiver, unmet caregiver needs and informal help received.Higher caregiver age was positively associated with perceived satisfaction of help received, but negatively associated with overall needs, total level of informal help received and help neededIn logistic regression analysis, caregiver gender and age accounted for 14% of variance in the likelihood of belonging to a particular caregiver group, with gender being the more significant predictor over ageAfter controlling for gender and age, caregiver needs were a significant predictor of the likelihood of belonging to a particular caregiver group, explaining 13% of varianceFTD caregivers had greater levels of needs compared to AD caregiversFTD caregivers reported at least 12 needs and a minimum of 6 unmet needs, AD caregivers reported at least 7 total needs, min. 2 unmet needsFTD caregivers reported significantly higher levels in 16 areas of needs, those were also more often perceived as unmetMemory concern was seen as an unmet need similarly in both groupsFTD caregivers required but also received a significantly greater amount of informal help than AD caregiversThe amount of formal help received was similar for both groupsCaregiver burden: female gender was significantly associated with greater overall strain, personal strain, and role strain; after controlling for age and gender, caregiver burden was not a predictor of belonging to a particular caregiver groupCaregiver anxiety and depression: neither anxiety nor depression were significantly correlated with age or gender and could not predict the likelihood of belonging to a particular caregiver groupDementia symptoms and caregiver reactions: no significant differences in the overall frequency of dementia symptoms and the caregiver reaction could be found between both groups, however there was a significant difference in the frequency of and the reaction towards disruptive behavior, with FTD caregivers scoring significantly higherFemale gender was positively associated with the frequency of disruptive symptoms and the reaction to them; caregiver age was positively correlated with the frequency of memory concerns and caregiver reaction to memory concernsDeterminants of caregiver distress: no group differences were found on overall DASS 21 scoresA regression analysis took diagnosis, relationship to patient, length of time caregiving, caregiver physical health (self-rated), ZBI scores into account as predictors for DASS 21 scores – a combination of all variables explained 49% of variance in caregiver distress, the only single significant predictor was caregiver burden, accounting for 31% of variance |
| Limitations | Selection biasSmall sample size |

### 1.1.28 Ng et al. (2012) – Severity of psychiatric symptoms correlates with activities of daily living and caregiver burden in frontotemporal dementia.

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| Reference | Ng, Amanda; Chua, Esther; Nyu, Mei Mei; Kandiah, Nagaendran (2012): Severity of psychiatric symptoms correlates with activities of daily living and caregiver burden in frontotemporal dementia. In: *Alzheimer's & Dementia* 8 (4), P568. DOI: 10.1016/j.jalz.2012.05.1535. |
| Type | Controlled cohort study, descriptive study (poster presentation) |
| Location/country | Singapore |
| Aim/subject | To assess the relationship between severity of neuropsychiatric symptoms and activities of daily living (ADL) as well as caregiver burden in FTD. |
| Participants | Recruitment from the National Neuroscience Institute dementia clinic, n=17 FTD patients with caregiversAge of patient (years): mean 60.06 (±7.01)Gender of patient: 29.41% maleEthnicity of patient: 88.24% Chinese |
| Methods/measures | Caregiver burden: assessed using the Screening for Caregiver Burden questionnaire (SCB)Behavioral symptoms and caregiver distress: assessed using the Neuropsychiatric Inventory Questionnaire (NPI-Q)ADL: assessed using the Alzheimer’s Disease Cooperative Study Group-Activities of Daily Living questionnaire (ADCS-ADL)  |
| Interventions | None |
| Outcomes | NPI-Severity and NPI-Distress subscales were positively correlated with SCB, ADCS-ADL scores (low scores indicating high dependency) were negatively correlated with SCBCaregiver burden increases with behavioral symptoms and dependency (lack of abilities in ADLs)  |
| Limitations | Lack of reported data, especially caregiver characteristicsSmall sample size |

### 1.1.29 Riedijk et al. (2006) – Caregiver burden, health-related quality of life and coping in dementia caregivers. A comparison of frontotemporal dementia and Alzheimer’s disease.

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| Reference | Riedijk, S. R.; Vugt, M. E. de; Duivenvoorden, H. J.; Niermeijer, M. F.; van Swieten, J. C.; Verhey, F. R. J.; Tibben, A. (2006): Caregiver burden, health-related quality of life and coping in dementia caregivers. A comparison of frontotemporal dementia and Alzheimer's disease. In: *Dementia and geriatric cognitive disorders* 22 (5-6), S. 405–412. DOI: 10.1159/000095750. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Netherlands |
| Aim/subject | To compare caregiver burden, health-related quality of life and coping strategies in caregivers of FTD and AD patients |
| Participants | FTD patients and caregivers: recruitment via yearly postal and telephone enquiries between January 1994 and June 2002 in nationwide outpatient clinics, data from FTD caregivers (diagnosis confirmed according to Lund-Manchester Criteria), usable results of 63 participants (response rate 72.4%)AD patients and caregivers: cohort from the Maastricht Study of Behavior in Dementia (MAASBED), AD diagnosis according to DSM-IV, 90 patient/caregiver dyadsDiagnosis of patient: 90 AD, 29 FTD living at home (FTDH), 34 FTD living in a nursing home (FTDN)Age of patient (years): AD mean 78.2 (±9.0), FTDH mean 60.0 (±8.6), FTDN mean 61.2 (±10.5)Gender of patient: AD 36% males, FTDH 38% males, FTDN 53% malesDuration of dementia (months): AD mean 42.3 (±29.8), FTDH mean 59.2 (±23.9), FTDN mean 98.4 (±42.6)Age of caregiver (years): AD mean 63.5 (±12.4), FTDH mean 57.1 (±10.7), FTDN mean 57.1 (±12.5)Gender of caregiver: AD 39% males, FTDH 55% males, FTDN 24% malesRelationship to patient: AD 52% spouses/48% children; FTDH 93% spouses/7% children; FTDN 71% spouses/29% children |
| Methods/measures | Neuropsychiatric disturbance: assessed using the Neuropsychiatric Inventory (NPI), maximum score of 10 subdomains = 120, distress maximum score = 50, Dutch versionCaregiver burden: assessed using the NPI-D score (see above), assessed using a visual analogue scale 0 (not at all)-10 (extremely)Caregiver health-related quality of life (HQoL): assessed using the Short Form 36 health survey (SF-36), Mental (MCS) and Physical Component Summary (PCS) scoresCaregiver coping styles: assessed using the Utrecht Coping List, measuring seven general coping styles in 44 items |
| Interventions | none |
| Outcomes | *FTDH vs AD*FTDH patients were significantly younger than AD patients and had a significantly longer disease durationFTDH patients experienced a significantly higher number and more severe (approximating significance) neuropsychiatric symptoms; FTDH patients exhibited especially euphoria, apathy, disinhibition, and aberrant motor behavior whereas AD patients significantly suffered from depressionIn comparison to AD caregivers, FTDH caregivers were significantly younger and significantly more often spouses; AD and FTDH caregivers did not differ in burden experienced by neuropsychiatric symptoms (NPI-D)FTDH caregivers felt significantly more burdened than AD caregivers; caregiver burden was predicted by seeking distraction as a coping strategy, anxiety and disinhibition as symptoms, explaining 31% of variance; the type of relationship to the patient did not influence caregiver burdenHQoL MCS scores were worst in caregivers of shortly demented AD patients and highest in older FTDH caregivers who had been demented for a longer time, MCS scores were predicted by the use of passive coping, explaining 37% of variance; no difference in PCS scoresNo significant difference in coping strategies between FTDH and AD caregivers, both using active coping and reassuring thoughts most often*FTDH vs FTDN*Duration of disease was significantly longer in FTDN patients compared to FTDH patientsFTDH patients experienced neuropsychiatric symptoms more frequently than FTDN patients, with most FTDH patients showing anxiety and irritability whereas FTDN patients were experiencing higher levels of apathyFTDH caregivers experienced higher burden associated with neuropsychiatric symptoms (NPI-D) than FTDN caregivers; FTDN caregivers of patients with a short duration of dementia were significantly more burdened (analogue scale), burden of caregiving was predicted by passive coping, explaining 25% of varianceFTDN caregivers had lower MCS scores than FTDH caregivers, caregivers of patients who had been demented for a shorter duration also scored lower on the MCS; MCS scores were predicted by passive coping, explaining 31% of variance; no significant differences in PCS scoresBoth FTDN and FTDH caregivers mostly used active coping strategies and reassuring thoughts, no significant differences were found |
| Limitations | No ADN group |

### 1.1.30 Riedijk et al. (2008) – Frontotemporal dementia. Change of familial caregiver burden and partner relation in a Dutch cohort of 63 patients.

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| Reference | Riedijk, Samantha; Duivenvoorden, Hugo; Rosso, Sonia; van Swieten, John; Niermeijer, Martinus; Tibben, Aad (2008): Frontotemporal dementia. Change of familial caregiver burden and partner relation in a Dutch cohort of 63 patients. In: *Dementia and geriatric cognitive disorders* 26 (5), S. 398–406. DOI: 10.1159/000164276. |
| Type | Controlled cohort study, descriptive study, longitudinal study |
| Location/country | Netherlands |
| Aim/subject | To assess the change of caregiver burden in FTD over a 2-year period. |
| Participants | FTD patients and caregivers: recruitment via yearly postal and telephone enquiries between January 1994 and June 2002 in nationwide outpatient clinics, data from FTD caregivers (diagnosis confirmed according to Lund-Manchester Criteria), usable results of 63 participants (response rate 72.4%), Data for 31 caregiver/patient dyads completed upon 24-month follow-upDiagnosis of patient: 29 FTD living at home (FTDH), 34 FTD living in a nursing home (FTDN)Age of patient (years): FTDH mean 60.0 (±8.6), FTDN mean 61.2 (±10.5), total mean 60.7 (±9.6)Gender of patient: FTDH 38% males, FTDN 53% males, total 62% males\*Duration of dementia (months): FTDH mean 59.2 (±23.9), FTDN mean 98.4 (±42.6), total mean 80.8 (±40.1)Age of caregiver (years): FTDH mean 57.1 (±10.7), FTDN mean 57.1 (±12.5), total mean 57.1 (±11.6)Gender of caregiver: FTDH 38% males, FTDN 53% males, total 38% males\*\*Relationship to patient: FTDH 93% spouses/7% children; FTDN 71% spouses/29% children; total 81% spouses/14% children\*Percentage does not match the actually reported number of males\*\*Data reported regarding caregiver gender does not match previously reported data of this cohort, percentage does not match the actually reported number |
| Methods/measures | Baseline (time 1): all measures6-month, 12-month and 18-month follow-up: Patient’s domicile, caregiver burden, physical health on visual analogue scale, mental health on visual analogue scale24-month follow-up (time 2): all measures (for details, see below)Behavioral problems and caregiver distress: assessed using the Neuropsychiatric Inventory (NPI), maximum score of 10 subdomains = 120, distress maximum score = 50, Dutch version, not completed upon follow-up if patient had deceasedDementia severity: assessed using the Global Deterioration Scale (GDS), dementia severity stages 1-7 (most severe impairment), not completed upon follow-up if patient had deceasedCaregiver burden: assessed using the NPI-D score (see above), assessed using a visual analogue scale 0 (not at all)-10 (extremely), also completed upon follow-up if patient had deceasedCaregiver health: assessed using dichotomous question whether they were currently suffering from physical or mental health problems at times 1 and 2; assessed at 6-month, 12-month and 18-month follow-up using a visual analogue scale for rating both health dimensions from 0 (extremely poor) to 10 (extremely well) & a dichotomous scale rating whether or not their health was influenced by caregivingCaregiver psychopathology: assessed using the 90-item Revised Symptom Checklist (SCL-90-R), assessing 8 dimensions of psychological symptoms, adding up to a general psychopathology scoreCaregiver health-related quality of life (HQoL): assessed using the Short Form 36 health survey (SF-36), Mental (MCS) and Physical Component Summary (PCS) scoresCaregiver coping styles: assessed using the Utrecht Coping List, measuring seven general coping styles in 44 itemsSocial support: assessed using the Social Support List (SSL) Quality of relationship to patient: assessed using a visual analogue scale from 0 (extremely poor) to 10 (extremely well), also used to assess premorbid relationship quality; assessed using four items of the University of Southern California Longitudinal Study of Three-Generation Families measures of positive affect |
| Interventions | None |
| Outcomes | *Patients*FTDH patients at time 2: 10 living at home, 7 moved to nursing home, 5 deceased, 7 lost to follow-upFTDN patients at time 2: 22 living in nursing home, 9 deceased, 3 lost to follow-upDementia severity increased significantly for all patients, with FTDH patients showing a significantly more rapid increase, even though their severity was significantly lower at baselineNeuropsychiatric symptoms showed a trend of decline and were negatively associated with dementia severity at time 2 (no association at time 1)*Caregivers*NPI-D scores decreased significantly from time 1 to time 2Caregiver burden tended to increase in FTDH caregivers, whereas FTDN caregivers and those of deceased patients tended to experience a decline in burdenBurden was highest in patients who were living at home at baseline but who moved into a nursing home during the follow-up and lowest in caregivers whose patients had deceased.Caregivers’ physical and mental health improved significantly, a negative influence of caregiving on health was reported less frequently at time 2.There was no significant change in psychological symptoms as measured on the SCL-90-R, no significant change on PCS and MCS were observed.Coping strategies were used to a similar degree over the 24 months of time, but with the coping style ‘depressive reaction’ increasing significantly. ‘Emotional expression’ was used significantly more by FTDN than by FTDH caregivers.Social support and negative interactions remained the same over time, caregivers experienced more instrumental support than negative interactions.Premorbid quality of relationship was rated significantly better than at baseline, but no change was observed over the 24-month period. The same applied for relationship components. |
| Limitations | Selective drop-outs may affect generalizabilityNo differentiation of FTD subtypesNo control group (AD cohort)Inconsistencies in reported data (Patient and caregiver gender) |

### 1.1.31 Riedijk et al. (2009) – Sense of competence in a Dutch sample of informal caregivers of frontotemporal dementia patients.

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| Reference | Riedijk, Samantha; Duivenvoorden, Hugo; van Swieten, John; Niermeijer, Martinus; Tibben, Aad (2009): Sense of competence in a Dutch sample of informal caregivers of frontotemporal dementia patients. In: *Dementia and geriatric cognitive disorders* 27 (4), S. 337–343. DOI: 10.1159/000207447. |
| Type | Controlled cohort study, descriptive study, longitudinal study |
| Location/country | Netherlands |
| Aim/subject | To assess the sense of competence (SC) in FTD caregivers and its impact on caregiver burden. |
| Participants | FTD patients and caregivers: recruitment via yearly postal and telephone enquiries between January 1994 and June 2002 in nationwide outpatient clinics, data from FTD caregivers (diagnosis confirmed according to Lund-Manchester Criteria), usable results of 63 participants (response rate 72.4%), 46 patient/caregiver dyads completed entire follow-upData at 24-month follow-up:Age of patient (years): mean 61.4 (±8.0)Gender of patient: 46% maleDuration of dementia (years): mean 8.1 (±2.8)Domicile of patient: 17% at home, 53% in nursing homes, 28% deceased, 2% unknownAge of caregiver (years): mean 59.1 (±8.0)Gender of caregiver: 43% maleRelationship to patient: 78% spouses, 18% children, 4% other |
| Methods/measures | Behavioral problems and caregiver distress: assessed using the Neuropsychiatric Inventory (NPI), maximum score of 10 subdomains = 120, burden maximum score = 19, Dutch version, not completed upon follow-up if patient had deceasedDementia severity: assessed using the Global Deterioration Scale (GDS), dementia severity stages 1-7 (most severe impairment), not completed upon follow-up if patient had deceasedCaregiver burden: assessed using the NPI-D score (see above), assessed using a visual analogue scale 0 (not at all)-10 (extremely), also completed upon follow-up if patient had deceasedCaregiver psychopathology: assessed using the 90-item Revised Symptom Checklist (SCL-90-R), assessing 8 dimensions of psychological symptoms, adding up to a general psychopathology scoreCaregiver health-related quality of life (HQoL): assessed using the Short Form 36 health survey (SF-36), Mental (MCS) and Physical Component Summary (PCS) scoresSense of Competence: assessed using the Sense of Competence Questionnaire (SCQ), higher scores indicating greater SC; one-dimensional scale ranging from 27 to 135; SCQ can furthermore be resolved into three dimensions, both approaches were applied in this study, SCQ was also completed at 24 months if the patient had deceased, referring to the time when the patient was still alive |
| Interventions | None |
| Outcomes | NPI total score showed no association to SCQ sum scoreThree principal components explained 49% of SCQ variance: ‘emotions’, ‘attributions’ and ‘sacrifice’SC dimensions not related to dementia severity; SC had no impact on general burden or NPI-burdenThe sacrifice component had the greatest impact in physical HQoL, effects on mental HQoL and psychological complaints were significant but lowerCaregivers generally felt competent about caring for the patient, expressed few negative emotions and attributions towards patients and their behaviorCaregivers felt worried about the patient a great part of the timeCaregivers experience a lack of time for their own personal life while providing care |
| Limitations | Drop-outs reduce generalizability No control group (AD cohort)No differentiation of FTD subtypes |

### 1.1.32 Riedl et al. (2014) – Long-term follow-up in primary progressive aphasia. Clinical course and health care utilisation.

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| Reference | Riedl, Lina; Last, Dirk; Danek, Adrian; Diehl-Schmid, Janine (2014): Long-term follow-up in primary progressive aphasia. Clinical course and health care utilisation. In: *Aphasiology* 28 (8-9), S. 981–992. DOI: 10.1080/02687038.2014.904497. |
| Type | Controlled cohort study, descriptive study, longitudinal study |
| Location/country | Munich, Germany |
| Aim/subject | To assess how PPA patients are cared for, what specific symptoms are relevant in caregiving and what support family caregivers seek. |
| Participants | Data of 43 PPA caregivers from a study including 144 FTLD caregivers from 2009/2010 (Diehl-Schmid et al., 2011) used, diagnosis according to Lund-Manchester criteria – differing slightly from criteria in use since 2011🡪 svPPA = SD, nfvPPA = PNFA, lvPPA not considered a PPA subgroup at time of recruitment 🡪 not included in the study, data of deceased patient also includedDiagnosis of patient: 21 SD, 22 PNFAAge of patient (years): mean 66.4 (±6.7)Gender of patient: 56% male/44% femaleDuration from onset to point of data collection (years): mean 8.3 (±3.7)Duration from diagnosis to point of data collection (years): mean 5.5 (±2.8)Age of caregiver (years): mean 66Gender of caregiver: 67% femaleCaregiver relationship to patient: 35 spouses/5 children/3 friendsLiving situation: 60% at home/40% in a nursing home |
| Methods/measures | Standardized telephone interview with caregiver about course of the disease, comorbidities, demographic data, health care utilization, living situation, symptoms, pharmacological and non-pharmacological treatmentFrequency and severity of behavioral disturbances: assessed using the Neuropsychiatric Inventory (NPI) |
| Interventions | None |
| Outcomes | 17 patients had been admitted to a nursing home; in 12% of cases, patients were declined admission or discharged from a nursing home because staff were unable to manage the symptomatology presented by patientsOf the 26 patients living at home, 58% of their caregivers had no support at all, 12% were regularly supported by friends or relatives, 31% received assistance from professional in-home nursing care, 15% had domestic aid, 12% of patients attended day-care on a regular basis, one patient (4%) received meals on wheels75% of patients received financial support from the long-term care insurance (German system of “Pflegestufen”)26% of caregivers had visited a support group at least once, no other support services were utilized |
| Limitations | Small sample sizeData based on subjective caregiver informationNo control group |

### 1.1.33 Roche et al. (2015) – The role of coping strategies in psychological outcomes for frontotemporal dementia caregivers.

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| Reference | Roche DClinPsy, Lauren; Croot, Karen; MacCann, Carolyn; Cramer, Barbara; Diehl-Schmid, Janine (2015): The Role of Coping Strategies in Psychological Outcomes for Frontotemporal Dementia Caregivers. In: *Journal of geriatric psychiatry and neurology* 28 (3), S. 218–228. DOI: 10.1177/0891988715588830. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Germany |
| Aim/subject | To assess coping strategies and their effect on psychological outcomes in FTD caregivers. |
| Participants | 200 questionnaires were sent to caregivers that were recruited from 4 German FTD caregiver support groups, 6 months were assigned for collecting data; a telephone interview with the aim of explaining and clarifying the content of the questionnaire was conducted immediately after the questionnaire was returned to the research center104 caregivers participated, 10 were excluded because patients had already diedDiagnosis of patient: 87.2% bvFTD, 12.8% lvFTD (SD or PNFA) Age of patient: mean 63.94 years Gender of patient: 64 male/30 femaleAge at diagnosis: mean 60.41 years (±9.89)Age of caregiver: mean 59.11 years Gender of caregiver: 26 male/68 femaleRelationship to patient: 79.8% spouses11.7% had a child younger than 21 years, 24.5% had limited financial means since FTD onset |
| Methods/measures | Also described in Diehl-Schmid et al. 2013Care intensity/caregiver burden: determined using German nursing care level (NCL) system, levels I-III, higher degrees indicating a decline in ADLs of patientsFinancial resources: assessed using a 5-point scale rating whether money is tight, reverse coded 🡪 higher scores indicating greater resourcesCaregiver strain: assessed using the Caregiver Strain Index, score of 7 out of 13 indicating high caregiver strainCaregiver depression: assessed using the Beck Depression Inventory Second Edition (BDI-II), maximum score 63, score ≥13 = mild depression, ≥20 = moderate, ≥29 = severeQuality of Life (QoL): assessed using the Quality of Life-Alzheimer’s Disease (QoL-AD) scale, higher scores indicating greater QoLCoping strategies: assessed using the Brief Coping Orientations to Problems Experiences (Brief COPE), 28 items rated on a 1 (not utilized) to 4 (utilized frequently) scaleStatistical analysis: three sets of analyses were developed; Set I = investigating caregiver strain as a mediator between NCL and caregiver depression and QoL, respectivelySet II = investigating coping strategies as a mediator of caregiver strainSet III = investigating coping strategies as mediators of caregiver strain and caregiver depression and QoL, respectively |
| Interventions | None |
| Outcomes | 72.4% of caregivers experienced a great level of strain according to the CSI, on average, caregivers also achieved scores indicating mild depression on the BDI-IICaregivers mainly used problem-focused coping, followed by emotion-focused coping and dysfunctional coping strategies Set I: The direct effect of NCL on depression was not significant, but the indirect effect with strain being a mediator reached significanceFor the effect of NCL on QoL, both the direct and the indirect effect with strain as a mediator were significantSet II: in the final step of multiple regression, greater dysfunctional coping, higher NCL, greater financial resources and the interaction between NCL and financial resources were determined as predictors of caregiver strain; the relationship between NCL and strain was stronger under the circumstance of low financial resourcesSet III: the direct effect for strain predicting depression was significant; so were the indirect effects when caregiver gender (female) and dysfunctional coping were regarded as a mediator, respectivelyThe direct effect for strain predicting QoL was significant; so were the indirect effects for caregiver age and problem-focused coping as mediators, respectivelyProblem- and emotion-oriented coping did not predict reduced caregiver strain; care intensity alone did not prove to be a good predictor of caregiver strain |
| Limitations | Selection biasNCL is a vague determinant for care intensity Exclusively self-report measuresCSI questionable for use in dementia caregiversNo differentiation of FTD subtypes |

### 1.1.34 Rosness et al. (2008) – Support to family carers of patients with frontotemporal dementia.

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| Reference | Rosness, Tor Atle; Haugen, Per Kristian; Engedal, Knut (2008): Support to family carers of patients with frontotemporal dementia. In: *Aging & mental health* 12 (4), S. 462–466. DOI: 10.1080/13607860802224334. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Norway |
| Aim/subject | To assess the provision of support for family caregivers in FTD in comparison with AD caregivers and their satisfaction with support provided. |
| Participants | Recruitment between 2002-2004 in five Norwegian counties, patients with age ≤64 and diagnosis of FTD (according to Lund-Manchester criteria) or early-onset AD (according to ICD-10 criteria) were invited to participate, Diagnosis of patient: 23 FTD; 37 ADAge of patient (years): FTD mean 59.5 (±4.0), AD mean 60.0 (±3.8)Gender of patient: FTD 73% females, AD 43% femalesCaregiver relationship to patient: FTD 61% spouses/26% children/13% other; AD 68% spouses/24% children/8% otherLiving situation: FTD 57% living at home/AD 78% living at homeChildren <18 years: FTD 35%, AD 24% |
| Methods/measures | Patient characteristics: also included information about employment and records at local authorities/police regarding misdemeanors as reported by the caregiver; behavioral change as observed by the caregiver, time from symptom onset until diagnosis, MMSE score at diagnosisCare provision: structured questionnaires covering the living situationCaregiver variables: apart from demographic variables, satisfaction was assessed for the areas of diagnosis, treatment, oral or written information provided by a specialist; guidance, counselling and follow-up at specialist health care services |
| Interventions | None |
| Outcomes | Less FTD patients were employed at the time of diagnosis, had a significantly longer duration between symptom onset and diagnosis, significantly more behavioral disturbances and more problems with local authorities than AD patients.The proportion of FTD patients attending a day-care center in comparison to AD patients approached significance, significantly more FTD patients had been admitted to stays in nursing homes (short- or long-term)FTD caregivers were significantly less satisfied with information provision in general as well as with counselling and follow-ups. |
| Limitations | Small sample sizeNo measure of caregiver burdenNo information about caregiver characteristics (e.g. age, gender) availableLack of information about assessment tools (validation etc.) |

### 1.1.35 Uflacker et al. (2015) – Caregiver burden in Prion disease as compared to frontotemporal dementia and Alzheimer disease.

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| Reference | Uflacker, Alice; Edmondson, Mary; Onyike, Chiadi; Appleby, Brian (2015): Caregiver Burden in Prion Disease as Compared to Frontotemporal Dementia and Alzheimer Disease. In: *The American Journal of Geriatric Psychiatry* 23 (3), S141-S142. DOI: 10.1016/j.jagp.2014.12.146. |
| Type | Retrospective cohort study, descriptive study (poster presentation) |
| Location/country | USA |
| Aim/subject | To compare caregiver burden in prion disease with burden in FTD and AD |
| Participants | 136 patients from the John Hopkins Frontotemporal and young Onset Dementia Clinic with diagnoses including bvFTD, lvFTD, AD and Prion Disease |
| Methods/measures | Data collected every 3-6 months for 5 yearsCaregiver burden: assessed using the Neuropsychiatric Inventory questionnaire (NPI-Q) distress scores, assessed using the Zarit Burden Inventory (ZBI)Depression: assessed using the Geriatric Depression Scale (GDS), assessed using the Cornell Scale for Depression in Dementia (CSDD)Apathy: assessed using the Apathy Evaluation Scale (AES)Activities of Daily Living: assessed using the Katz Index of Independence in Activities of Daily Living (Katz), assessed using the Lawton and Brody Instrumental Activities of Daily Living ScaleDementia: assessed using the Clinical Dementia Rating Scale (CDR), assessed using the Unified Parkinson’s Disease Rating Scale-II (UPDRS-II) |
| Interventions | None |
| Outcomes | Caregiver burden was higher in Prion disease when compared to AD, but comparable to caregiver burden in bvFTD |
| Limitations | Lack of reported data (patient and caregiver characteristics) |

### 1.1.36 Uflacker et al. (2016) – Caregiver burden in atypical dementias. Comparing frontotemporal dementia, Creutzfeldt-Jakob disease, and Alzheimer’s disease.

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| Reference | Uflacker, Alice; Edmondson, Mary C.; Onyike, Chiadi U.; Appleby, Brian S. (2016): Caregiver burden in atypical dementias. Comparing frontotemporal dementia, Creutzfeldt-Jakob disease, and Alzheimer's disease. In: *International psychogeriatrics* 28 (2), S. 269–273. DOI: 10.1017/S1041610215001647. |
| Type | Controlled comparative study, descriptive study |
| Location/country | USA |
| Aim/subject | To compare burden among caregivers of FTD, young-onset AD and Creutzfeldt-Jakob disease (sCJD) patients |
| Participants | A total of 223 patients seen at John Hopkins Frontotemporal and young Onset Dementia Clinic, patients without ZBI scores or alternative diagnosis excluded, AD according to NINCDS-ADRDA criteria, FTD according to Neary criteria, sCJD according to MRI-CJD criteria, 76 patients in totalDiagnosis of patient: 21 AD, 33 bvFTD, 15 lvFTD, 7 sCJDPatient age at onset (years): AD mean 57 (±8.5), bvFTD mean 57 (±10), lvFTD mean 62 (±7.1), sCJD mean 60 (±10)Gender of patient: AD 48% male, bvFTD 64% male, lvFTD 40% male, sCJD 71% maleLiving at home: AD 90%, bvFTD 97%, lvFTD 100%, sCJD 86% Survival time (months): AD n/a, bvFTD 94 (±37), lvFTD n/a, sCJD 21 (±9) |
| Methods/measures | Caregiver burden: assessed using the short Zarit Burden Interview (ZBI)Neuropsychiatric symptoms: assessed using the Neuropsychiatric Inventory questionnaire (NPI-Q)Patient’s daily functioning: assessed using the Clinical Dementia Rating Scale (CDR)Patient’s cognition: assessed using the Mini Mental State Exam (MMSE)Patient’s motor impairments: assessed using the Unified Parkinson’s Disease Rating Scale-II (UPDRS-II) |
| Interventions | None |
| Outcomes | Burden tended to be greater in bvFTD compared to AD caregiverssCJD patients had a significantly shorter survival time than bvFTD patients, no data available for AD and lvFTD patients because no patient had deceased upon closing of the studyLiving arrangements did not impact ZBI scoresNPI-Q distress scores, number of symptoms and severity of symptoms were significantly higher in bvFTD and sCJD compared to ADbvFTD patients showed significantly higher apathy and disinhibition than AD patientsIn regression analyses, Diagnosis × NPI-Q total severity score showed a significant effect on ZBI scores in sCJD and bvFTD patients |
| Limitations | Small sample sizeUse of MMSE in FTD patients questionable (Piguet et al. 2013)No information about caregiver characteristics (e.g. age, gender) available |

### 1.1.37 Vugt et al. (2006) – Impact of behavioral problems on spousal caregivers. A comparison between Alzheimer’s disease and frontotemporal dementia.

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| Reference | Vugt, Marjolein E. de; Riedijk, Samantha R.; Aalten, Pauline; Tibben, Aad; van Swieten, John C.; Verhey, Frans R. J. (2006): Impact of behavioral problems on spousal caregivers. A comparison between Alzheimer's disease and frontotemporal dementia. In: *Dementia and geriatric cognitive disorders* 22 (1), S. 35–41. DOI: 10.1159/000093102. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Netherlands |
| Aim/subject | To assess the impact of behavioral problems on spouses that provide care for FTD patients in comparison to AD: |
| Participants | AD patients from the Maastricht Study if Behavior in Dementia (MAASBED) cohort, diagnosis according to DSM-IV criteria; FTD patient’s diagnosis according to Lund and Manchester criteriaDiagnosis of patient: 47 AD, 27 FTDAge of patient (years): AD mean 71.5 (±8.2), FTD mean 59.5 (±8.4)Gender of patient: AD 28 male/19 female, FTD 15 male/12 femaleDuration of disease (months): AD mean 39.7 (±28.5), FTD mean 60.5 (±24.3)Age of caregiver (years): AD mean 71.3 (±8.6), FTD mean 58.5 (±9.6)Gender of caregiver: AD 20 male/27 female, FTD 11 male/16 female |
| Methods/measures | Behavioral problems: assessed using the Neuropsychiatric Inventory (NPI), NPI-Distress score for assessing distress caused by symptoms, Dutch versionCognitive functioning: assessed using the Mini Mental State Exam (MMSE)ADL: assessed using the Interview for Deterioration in Daily living activities in Dementia (IDDD), performance score range 0-44, initiation score range 0-36Caregiver distress: assessed using the NPI-Distress score, assessed using a visual analogue scale ranging from 1 to 10Caregiver competence: assessed using the Short Sense of Competence Questionnaire (SSCQ) |
| Interventions | none |
| Outcomes | FTD patients and caregivers were significantly younger, disease duration was longer, cognitive functioning and initiating ADLs was worse than in AD patientsBehavioral symptoms were present in 100% of FTD patients and 91% of AD patients; apathy was the most common symptoms in both groups but occurred more often in FTD; next most frequent symptoms in FTD were aberrant motor behavior, disinhibition and irritabilityFTD patients had significantly higher NPI total scores and higher subscale scores in agitation, euphoria, apathy, disinhibition and aberrant motor behavior; these differences remained significant except for euphoria even after controlling for disease severity (IDDD scores); after controlling also for MMSE, only disinhibition and aberrant motor behavior remained significantMost distressing symptoms in FTD were apathy and disinhibition; euphoria and disinhibition were significantly more distressing for FTD caregivers, this difference remained significant for disinhibition after controlling for IDDD performance, caregiver age and MMSE scoresCaregivers of FTD patients experienced significantly more distress on the visual analogue scale, no difference in total SSCQ scores, on subscale scores FTD caregivers were less satisfied with the patient as the recipient and themselves as caregiversDisinhibition was experienced as highly distressing in FTD caregivers, depression was less frequent in FTD patients than in AD, but was experienced as highly distressing by caregivers |
| Limitations | Selection biasOther factors than caregiver age should be taken into account for adjustmentUse of MMSE in FTD patients questionable (Piguet et al. 2013) |

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### 1.1.38 Wong, Wallhagen (2012) – Frontotemporal dementia: the impact of behavioral symptoms on the physical and mental health of family caregivers.

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| Reference | Wong, Cindy C.; Wallhagen, Margaret I. (2012): Frontotemporal dementia: the impact of patient behavioral symptoms on the physical and mental health of family caregivers. In: *Dementia and geriatric cognitive disorders extra* 2 (1), S. 516–528. DOI: 10.1159/000345082. |
| Type | Controlled cohort study, descriptive study |
| Location/country | USA |
| Aim/subject | To assess the impact of behavioral symptoms in FTD patients on caregiver’s physical and mental health. |
| Participants | Recruitment from support groups that were associated with dementia clinics, especially in Portland, Oregon and San Francisco, California, as well as the Association for Frontotemporal Degeneration and their website between June and November 2011;Inclusion criteria: primary family caregiver, at least 6 months of care, living with the patient, no financial compensation for care, sufficient proficiency in English, ≥18 years of age; patients had to be diagnosed with FTD with behavioral problems as reported by the caregiver61 caregiver/patient dyadsAge of patient (years): mean 65.79 (±9.35)Gender of patient: 67.2% male/328% femaleRace/ethnicity of the patient: 95.1% Caucasian/White, 1.6% African-American/Black, 1.6% Hispanic, 1.6% ChineseYears since diagnosis: mean 4.45 (±2.49)Age of caregiver (years): mean 61.85 (±10.83)Gender of caregiver: 21.3% male/78.7% femaleRelationship to patient: 90.2% partner, 6.6% daughter, 3.3% otherRace/ethnicity: 93.4% Caucasian/White, 1.6% African-American/Black, 1.6% Hispanic, 3.7% ChineseDuration caregiver has known patient (years): mean 39.39 (±13.83)Duration of caregiving (years): mean 5.96 (±8.03) |
| Methods/measures | Assessment tools were self-completed in the form of a postal surveyCaregiver health: assessed using the Short Form Health Survey (SF-12), yielding two subscores, the Physical component summary (PCS) and the Mental component summary (MCS)Patient Neuropsychiatric Symptoms: assessed using the Neuropsychiatric Inventory Questionnaire (NPI-Q), symptom severity score range 0-36, higher scores indicating greater severity; caregiver distress score range 0-60, higher scores indicating higher caregiver distress;to assess other symptoms common in bvFTD which are not covered by the NPI-Q, 8 additional questions regarding loss of insight, social inappropriateness, social avoidance, criminal behavior, hypersexuality, hyposexuality, preference for sweets, perseverations/obsessions; severity score range 0-24, distress score range 0-40 for the additional questions |
| Interventions | None |
| Outcomes | Caregiver characteristics: 52.5% of caregivers did not receive any form of paid support, 43% received paid support on 1-2 days/week; 47.5% of caregivers were not receiving any kind of unpaid support from friends or relatives, 44% were receiving unpaid support on 1-2 days/weekPatient Neuropsychiatric Symptoms and Behavioral Problems: 84% of patients exhibited apathy/indifference; 75% showed loss of insight, 75% appetite/eating problems, 67% social inappropriateness, 64% perseverations/obsessions, 64% disinhibition;Apathy/indifference and loss of insight were most distressing for caregiversElation/euphoria (25%), hallucinations (25%), hypersexuality (15%) and criminal behavior (10%) were reported less oftenCorrelations between neuropsychiatric symptoms and caregiver health: significant positive relationships were observed between NPI-Q severity scores, NPI-Q distress scores, additional NPI-Q severity scores and additional NPI-Q distress scores.NPI-Q severity scores, additional NPI-Q severity scores and additional NPI-Q distress scores each showed a small significant negative correlation to MCS scores; the negative correlation between NPI-Q distress scores and MCS scores was mediumNone of the (additional) NPI-Q scores was significantly related to PCS scoresMultiple regression analyses: Analysis 1 (MR1) investigated the association between NPI-Q severity scores and MCS scores with further independent variables being caregiver age, years the caregiver had known the patient and time of care that had been provided, those 4 independent variables explained 34.5% of variance, the model was significant, only caregiver age made a significant unique contribution, explaining 9% of the variability, the NPI-Q severity scores not being significant and explaining only 1.6% MR 2 used caregiver age, years the caregiver had known the patient and time of care that had been provided as well as NPI-Q distress scores as the independent variables and MCS scores as the dependent variable; the model was significant and explained about 42.3% of variance; the NPI-Q distress score made a significant unique contribution and explained about 9.5% of variance, caregiver age also made a significant unique contribution and explained about 6.6% of variance |
| Limitations | Selection biasUnknown criteria of FTD diagnosis since survey was anonymous |

### 1.1.39 Wong and Wallhagen (2014) – Family caregivers of individuals with frontotemporal dementia: examining the relationship between coping and caregiver physical and mental health.

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| Reference | Wong, Cindy C.; Wallhagen, Margaret I. (2014): Family caregivers of individuals with frontotemporal dementia: examining the relationship between coping and caregiver physical and mental health. In: *Journal of gerontological nursing* 40 (1), S. 30–40. DOI: 10.3928/00989134-20130827-05. |
| Type | Controlled cohort study, descriptive study |
| Location/country | USA |
| Aim/subject | To assess the relationship between coping strategies and physical and mental health in caregivers of FTD patients. |
| Participants | Recruitment between June and November 2011, 61 caregivers of FTD patients, inclusion criteria: primary caregiver, living with the patient, having provided care for at least 6 months, no financial compensation for caregiving, proficiency in English, be 18 or older; self-administered questionnairesAge of patient (years): mean 65.79 (±9.35), range 38 to 88Gender of patient: 67.2% maleRace/ethinicity of patient: 95.1% Caucasian/WhiteTime since diagnosis (years): mean 4.45 (±2.49), range 1 to 12Age of caregivers (years): mean 61.85 (±10.83), range 35 to 90Gender of caregiver: 78.7% femaleRelationship to patient: 90.2% spouses, 6.6% children, 3.3% otherRace/ethnicity of caregiver: 93.4% Caucasian/White |
| Methods/measures | Coping strategies: assessed using the Brief COPE scale Caregiver Relationship satisfaction: assessed using the Couples Satisfaction Index (CSI-4)Patient Neuropsychiatric Symptoms: assessed using the Neuropsychiatric Inventory Questionnaire (NPI-Q)Caregiver Physical and Mental Health: assessed using the 12-item Short-Form Health Survey (SF-12), yielding a Physical Component Summary (PCS) and the Mental Component Summary (MCS) |
| Interventions | none |
| Outcomes | Caregivers most often used acceptance, active coping and planning as coping strategies; behavioral disengagement and denial were used leastDysfunctional coping was significantly negatively related with caregiver age and caregiver relationship satisfactionEmotion-oriented coping was associated with CSI scores, problem-focused coping was associated with PCS scoresMultiple regression analysis for association between emotion-focused coping and caregiver mental health after controlling for caregiver age, gender and relationship satisfaction showed that 43% of variance were explained by the statistically significant model, emotion-focused coping and alone explained 9.7%, caregiver age 32%The second regression model examined the association between problem-focused coping and caregiver physical health after controlling for caregiver age, gender and relationship satisfaction; 24% of variance were explained by the statistically significant model, independent significant contributions were made by problem-focused coping (9.54%) and CSI (11.16%)Statistically significant gender differences observed in the domains of emotion-oriented and problem-focused coping, used more by women; no significant differences observed in dysfunctional coping, although also used more by women. |
| Limitations | Selection biasUnknown criteria of FTD diagnosis since survey was anonymousCSI questionable for use in dementia caregivers |

## 1.2 ALS/MND

### 1.2.1 Andrews et al. (2017) – Which behaviors? Identifying the most common and burdensome behavior changes in amyotrophic lateral sclerosis.

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| Reference  | Andrews, Sophie Claire; Pavlis, Alexia; Staios, Mathew; Fisher, Fiona (2017): Which behaviors? Identifying the most common and burdensome behavior changes in amyotrophic lateral sclerosis. In: *Psychology, health & medicine* 22 (4), S. 483–492. DOI: 10.1080/13548506.2016.1164871. |
| Type | Controlled comparative study, descriptive study |
| Location/Country | Melbourne, Australia |
| Aim/subject | To assess difficulties in functional and behavioral domains in ALS patients compared to demographically matched healthy control group using ratings of informants; to examine the relationship between these difficulties and caregiver burden |
| Participants | 40 ALS participants and their caregiversdiagnosis of probable or definite ALS as defined by El Escorial criteriaexclusion of patients with significant respiratory involvement (FVC <70%), recruitment via specialist ALS clinic27 healthy control group (CG) participants with their significant othersGeneral exclusion criteria: previous or current neurological or psychiatric disease, head injury, other disease that is known to affect CNS function; Non-English speakers; significant hearing impairmentAge of participants: ALS mean 65.64 years ±10.53 (range 31-86); CG mean 63.94 ± 10.83 (range 35-80)Gender of participants: ALS 22 male/ 18 female; CG 13 male/ 14 femaleMean years of education in participants: ALS 12.40 years ±2.05; CG 13.22 ±2.64Mean months since symptom onset in ALS patients: 25.55 ±14.18Mean ALSFRS-R score: 35.25 (SD = 8.86, range 12-46)Age of caregivers: ALS mean 56.05 years ±14.49 (range 27-82); CG mean 57.08 ±16.24 (range 28-80)Gender of caregivers: ALS 9 male/31 female; CG 8 male/19 female |
| Methods/measures | Cambridge Behavioral Inventory Revised (CBI-R): used to measure behavioral disturbances, total score (max. 180), scores converted into percentage of impairment: 0% absent, 1-25% mild, 26-50% moderate, 51-75% severe, 76-100% very severecompleted by ALS and CG informantsALS Functional Rating Scale Revised (ALSFRS-R): physician-generated estimate of patients’ impairment, higher scores indicate better function, total score of 48 (= normal function)completed by treating neurologist in ALS clinic for ALS patientsZarit Burden Interview (ZBI): used to measure caregiver burden with 22 items, total score of 88; ≤8 low burden, 9-17 moderate burden, 18-32 high burden, ≥33 severe burdenCompleted by ALS informantsGender, age, education, occupation and medical history information collected for all participantsALS diagnosis and onset information collected for ALS patients, ALS phenotype determined by treating neurologist |
| Interventions | None |
| Outcomes | CBI-R: significantly more disturbances in ALS patients reported in subdomains of everyday skills, self-care, sleep (50-60% moderate-severe), mood (25% moderate-severe), motivation (30% moderate-severe); more frequent abnormal behavior (e.g. disinhibition, impulsivity) suggested to be occurring in ALS group (*p* = .04); no significant difference in domains of memory and orientation, odd beliefs, eating habits, stereotypic and motor behaviors (nevertheless up to 25% of ALS patients rated as moderate-severe) in comparison with CGZBI: 25% high or severe levels of burden, 37.5% moderate, 37.5% low No association of functional impairment (ALSFRS-R scores) with increased caregiver burden; CBI-R total score positively correlated with caregiver burden; subdomains of memory and orientation, everyday skills and motivation related to caregiver burden; no significant association found between other domains and caregiver burden Mood issues and apathy, but not other hallmark features of bvFTD like such as abnormal eating behaviors were found in ALS patients |
| Limitations | Small sample sizeALS-bvFTD cases may be underrepresentedSubjective measurement of behavioral function, no additional objective measures such as e.g. memory testingNo measurement of executive functions |

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### 1.2.2 Bock et al. (2016) Cognitive-behavioral changes in amyotrophic lateral sclerosis. Screening prevalence and impact on patients and caregivers.

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| Reference | Bock, Meredith; Duong, Y-Nhy; Kim, Anthony; Allen, Isabel; Murphy, Jennifer; Lomen-Hoerth, Catherine (2016): Cognitive-behavioral changes in amyotrophic lateral sclerosis. Screening prevalence and impact on patients and caregivers. In: *Amyotrophic lateral sclerosis & frontotemporal degeneration* 17 (5-6), S. 366–373. DOI: 10.3109/21678421.2016.1165257. |
| Type | Controlled cohort study, descriptive study |
| Location/country | California, USA |
| Aim/subject | To assess the association between cognitive-behavioral deficits and disease stage, patient quality of life (QoL) and caregiver burden in ALS patients |
| Participants | All patients with a scheduled appointment at University of California, San Francisco (UCSF) ALS Center between July 2014 and January 2015 were screened for eligibility and invited for participation if found eligible; inclusion criteria: definite, probable or possible ALS according to El Escorial criteria; exclusion criteria: lack of English language fluency, lack of caregiver who had known patient before ALS onset, premorbid non-FTD dementia, comorbid neurological diagnosis, new ALS diagnosis on the day of enrollment141 eligible patients, 91 agreed to participate; 5 drop-outs 🡪 86 participants, 31 were unable to complete the written fluency test (see below)Patients stratified by cognitive and behavioral status: 24 normal, 58 ALS-Ci (cognitive impairment) and ALS-Bi (behavioral impairment), 4 ALS-FTD (possible dementia with both cognitive and behavioral impairment)Age of patient: normal mean 62.3 years (SD 10.3), ALS-Ci & ALS-Bi mean 64.1 (SD 9.5), ALS-FTD mean 68 (SD 19.3)Gender of patient: 50 male/36 femaleRace of patient: 60 Caucasian, 8 Asian, 1 African American, 1 American Indian, 16 UnknownALS Region of onset: 26 arm, 31 leg, 8 trunk, 20 bulbar, 1 respiratoryVentilator status of patient: 56 none, 27 non-invasive, 3 invasiveFeeding method of patient: 73 oral intake, 13 percutaneous endoscopic gastrectomy (PEG) tubeYears of education in patient: normal mean 17.9 (SD 3.5), ALS-Ci & ALS-Bi mean 14.9 (SD 2.6), ALS-FTD mean 15.7 (SD 3.1)Symptom duration in months: normal mean 44.8 (SD 54.3), ALS-Ci & ALS-Bi mean 49.8 (SD 47.7), ALS-FTD mean 25.5 (17.3)ALS functional rating scale – revised score (range 0-48, 48 = most functional): normal mean 38.0 (SD 8.7), ALS-Ci & ALS-Bi mean 28.8 (SD 11.1), ALS-FTD mean 31.7 (11.1)Demographic and clinical characteristics abstracted from electronic medical record; education level based on self-report |
| Methods/measures | Cognitive function: assessed using ALS Cognitive-Behavioral Screen™ (ALS-CBS) Cognitive Subscale, score range 0-20, a score of 20 indicating least impairment; additionally, a written fluency test was assigned 🡪 classification of patient as cognitively normal, impaired (ALSci) or possible FTD-level impairmentBehavioral function: assessed using ALS-CBS caregiver survey component, score range 0-45, a score of 45 indicating least impairment 🡪 classification of patient as behaviorally normal, impaired (ALSbi) or possible bvFTDDisease severity: assessed using ALS Functional Rating Scale-Revised (ALSFRS-R), score range 0-48, a score of 48 indicating highest functionality Pseudobulbar affect: assessed using Center for Neurologic Study Lability Scale (CNS-LS), self-reported measure about uncontrollable or inappropriate laughing or crying, score range 8-45, a score of 45 indicating most symptomsDepressive symptoms: assessed using Geriatric Depression Scale (GDS), score range 0-15, a score of 15 indicating most symptomsQuality of Life: assessed using McGill Quality of Life-Single Item Score (MQoL-SIS), score range 0-10, a score of 10 indicating best QoLCaregiver burden: assessed using Caregiver Burden Scale (CGBS), score range 22-88, a score of 88 indicating the highest burden  |
| Interventions | None |
| Outcomes | Measure validation: a greater impairment on the cognitive ALS-CBS sub-score correlated with worse performance on the written fluency test, advanced disease ALSFRS-R scores correlated with increased disease duration and lower FVC, no significant variability in ALS-CBS scores between two administering study staff members or between three clinic sitesCognitive and behavioral impairment: higher educational level correlated with better cognitive scores, no association with behavioral scoresPredictors of QoL: no significant association between cognitive or behavioral impairment and QoL, higher GDS scores significantly associated with lower QoL, self-reported memory problems on the GDS did not correlate with a significantly lower ALS-CBS cognitive sub-scoreDepression and apathy: 73 patients fully completed GDS, 11 meeting criteria for probable depression (6 treated with antidepressant medication), 26 possible depression (12 treated with antidepressant) and 36 normal (10 treated with antidepressant); no significant association between self-reported depressive symptoms and caregiver-reported apathy; self-reported decreased interest in social surroundings, less emotional responsiveness and social withdrawal did not correlate significantly with higher self-reported depression symptomsPredictors of caregiver burden (CB): greater cognitive impairment on the ALS-CBS cognitive subscore was significantly associated with higher CB on CGBS scores, especially ‘poor attention and concentration’ being associated with higher CB, no significant association between fluency score and CB; caregiver-reported behavioral problems on ALS-CBS behavioral subscale significantly correlated with higher CB, 11 of 15 frontal lobe-mediated behavioral symptoms correlated independently with higher CB; worse function on ALSFRS-R scale in a model including behavioral status correlated with higher CB, no such significant correlation in a model including cognitive statusPredictors of disease stage: no association between cognitive or behavioral scores and disease stage as measured by ALSFRS-R Analysis after excluding possible FTD patients: no significant change in variables associated with QoL or ALSFRS-R; ALS-CBS cognitive sub-score was no longer significantly associated with CB (behavioral sub-score relationship to CB remained significant)Behavioral changes highly influenced caregiver burden, so did extreme cognitive changes (here only to be seen in possible FTD) which could imply the cause of caregiver burden being frontal lobe degeneration per se and not harsher caregiver rating of behavioral symptoms on the ALS-CBS; attention and concentration deficits could be screened for identifying higher caregiver burden and thus more extensive support, CB is likely to increase over the course of the disease |
| Limitations | ALS patient group may not be representative, self-perceived cognitive impairments might have led eligible patients to not participate and therefore not undergo cognitive testingALS-CBS tool cannot be considered diagnosticMQoL-SIS cannot represent disease-specific factors in QoLAvailable predictors accounted for ≤50% of observed variation in QoL and CB, thus other predictors should be identified and examinedNo information about caregiver characteristics (e.g. age, gender) available |

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### 1.2.3 Chiò et al. (2010) – Neurobehavioral symptoms in ALS are negatively related to caregivers’ burden and quality of life.

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| Reference | Chio, A.; Vignola, A.; Mastro, E.; Dei Giudici, A.; Iazzolino, B.; Calvo, A. et al. (2010): Neurobehavioral symptoms in ALS are negatively related to caregivers' burden and quality of life. In: *European journal of neurology* 17 (10), S. 1298–1303. DOI: 10.1111/j.1468-1331.2010.03016.x. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Torino, Italy |
| Aim/subject | To assess the frequency of neurobehavioral symptoms in ALS patients and their effect on patients’ and caregivers’ mood, burden and quality of life (QoL) |
| Participants | 70 patient/caregiver dyads at ALS clinic interviewed separatelyInclusion criteria: diagnosis of definite, probable or probable laboratory-supported ALS according to El Escorial criteria, informal caregiverExclusion criteria: positive family history for ALS, paid caregiverNo patient had SOD1 or TARDBO gene mutationsAge of patient: mean 61.9 years (±10.0)Gender of patient: 37 male/33 femaleEducational level of patients: mean 10.1 years (±4.7)Region of ALS onset: 54 spinal, 16 bulbarDisease duration: mean 16.5 months (±9.3)ALS-FRS score (see below): mean 29.2 (±6.1)MMSE score: mean 28.4 (±1.8, range 26-30, median 29)Patient ZDS score: mean 42.1 (±9.6), 9 patients with scores between 50 and 59 indicating mild depression, 6 patients with scores between 60 and 69 (moderate depression)Age of caregiver: mean 54.7 years (±13.3)Gender of caregiver: 23 male/47 femaleEducational level of caregiver: mean 11.0 years (±4.8)Relationship to patient: 56 spouses, 11 children, 3 other relativesCaregiver ZDS score: mean 39.1 (±7.6), 8 caregivers with scores between 50 and 59, none over 59 |
| Methods/measures | Behavioral abnormalities: assessed using the Frontal Systems Behavior Scale (FrSBe), validated Italian version, *T*-score composed of self-rated and family (caregiver)-rated questions regarding behavioral symptoms before onset of the disease and at present time, three subscales: apathy, disinhibition, executive dysfunction, *T*-score matched with gender, age and education; scores between 60 and 64 are considered borderline, scores ≥65 indicate frontal systems abnormalitiesCognitive function: assessed using the Mini Mental State Exam (MMSE), score range 0-30, higher scores indicating better cognitive function, corrected for age and education according to Italian normsDepression: assessed using the Zung Depression Scale (ZDS), self-reported scale, score range 20-80, scores 50 to 59 = mild depression, 60 to 69 = moderate depression, ≥70 = severe depression, administered to patients and caregiversQuality of Life: assessed using the McGill Quality of Life Questionnaire (MQoL), 16 items rated from 0-10, and MQoL-single item scale (MQoL-SIS), rating quality of life during the past 2 days, score range 0-10, a score of 10 indicating excellent QoL, administered to patients and caregiversCaregiver burden: assessed using the Caregiver burden inventory (CBI), self-administered, score range 0-100, a score of 100 indicating highest burdenPatients’ physical status: assessed using the ALS Functional Rating Scale (ALS-FRS), score range 0-40, higher scores indicating better function |
| Interventions | None |
| Outcomes | Frequency of neurobehavioral symptoms: caregivers of 15 patients reported of premorbid pathological scores on the FrSBe vs. 2 patients self-reporting premorbid pathological scoresCaregivers of 34 patients reported of present-time pathological scores vs. 9 patients self-reporting present-time pathological scores on the FrSBeCaregivers reported overall higher *T*-scores than patients, however there was a correlation between both ratingsCaregivers reported mostly of apathy as a present-time symptom in 39 patients, executive dysfunction in 32 patients and disinhibition in 18 patientsPatients’ self-rating reported of executive dysfunction in 14 patients, disinhibition in 7, apathy in 6Symptoms were not related to patients’ age, gender or ALS-FRS scorePresent-time bulbar symptoms were associated with a significantly higher FrSBe total score as well as apathy and executive dysfunction sub-scoresPatients’ ZDS was not significantly correlated with either patient- or caregiver-rated apathy scoresCorrelation between neurobehavioral symptoms and caregiver strain and QoL: caregiver depression and caregiver burden were both significantly correlated with patients’ total FrSBe scores as reported by the caregiver, apathy and executive dysfunction scores but not disinhibitionCaregiver QoL was correlated to FrSBe total score and all three componentsMultivariable analysis: caregiver depression independently related to MQoL score, FrSBe executive dysfunction domain, female caregiver; caregiver QoL was related to ZDS score and FrSBe total score; caregiver burden was related to FrSBe total score and ZDS scoreCorrelation between patients’ self-rated neurobehavioral symptoms and patients’ depression and QoL: no correlation between patients’ MQoL or ZDS scores and neurobehavioral symptoms |
| Limitations | No objective evaluation of executive dysfunctionNo specification of ALS-FTD diagnoses Use of MMSE in FTD patients questionable (Piguet et al. 2013) |

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### 1.2.4 Cui et al. (2015) – Behavioral symptoms in Motor Neuron Disease and their negative impact on caregiver burden.

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| Reference | Cui, Bo; Cui, Li-Ying; Liu, Ming-Sheng; Li, Xiao-Guang; Ma, Jun-Fang; Fang, Jia; Ding, Qing-Yun (2015): Behavioral Symptoms in Motor Neuron Disease and Their Negative Impact on Caregiver Burden. In: *Chinese medical journal* 128 (17), S. 2295–2300. DOI: 10.4103/0366-6999.163393. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Beijing, China |
| Aim/subject | To assess the distribution of abnormal behavior in Chinese ALS/MND patients and their impact on caregiver burden |
| Participants | One-hundred-eighteen patients enrolled at Peking Union Medical College Hospital and underwent neurological, laboratory, neuroimaging and electrophysiological examinations; diagnosis confirmed by three ALS/MND specialists, recruitment between February and December 2014, caregivers were invited to participate in caregiver burden assessment, 71 caregivers responded, after exclusion 65 patients and their caregivers were included in the final analysis;Exclusion criteria: concomitant neurological condition, alcohol- or drug-dependence, severe active mental illness, use of high-dose psychoactive medication, invasive ventilation support, paid caregiver, underage caregiverAge of patient: mean 50.9 years (±9.8)Gender of patient: 69.2% male/ 30.8% femaleDiagnosis of patient: 56 ALS/MND (according to El Escorial criteria), 9 progressive muscular atrophyDisease duration: median 12 months (IQR 7-20 months)Region of onset: 76.9% limb, 23.1% bulbarALSFRS-R score: median 42 (IQR 36-44)Age of caregiver: mean 41.5 years (±11.9)Relationship to patient: 38 spouses, 24 children, 2 siblings, 1 parentNo patients with positive family history of ALS/MND or dementia, no patients with gastrostomy or noninvasive ventilation |
| Methods/measures | General function: assessed using the ALS Functional Rating Scale-Revised (ALSFRS-R), score range 0-48, higher scores indicating better functionBulbar function: assessed using the swallowing subscale of the ALS severity scale (ALSSS), score range 0-10, lower scores indicating worse swallowing functionBehavioral change: assessed using the Frontal Behavioral Inventory-ALS version (FBI-ALS), two subscales (negative and disinhibition), score range 0-72, 0 = no behavioral change, 1-3 = mild, 4-14 moderate, ≥15 severe behavioral change, administered to caregiversFrontal cognitive function: assessed using the Frontal Assessment Battery (FAB), FAB score adjusted for age and level of educationCaregiver burden: assessed using the Caregiver Burden Inventory (CBI), score range 0-96, higher scores indicating more sever caregiver burden |
| Interventions | None |
| Outcomes | Abnormal behaviors: the three behavioral changes exhibited with the highest frequency were irritability (16 patients), logopenia (13 patients) and inflexibility (10 patients)37 patients did not exhibit behavioral change ( score = 0), 16 showed signs of mild change, 11 of moderate change and 1 of severe behavioral change – the patient with severe change also fulfilled diagnostic criteria for bvFTD, patients with moderate and severe change were subsumed as one of three behavioral patient groups, these groups did not differ significantly in clinical or sociodemographic variables except for the swallowing subscale of the ALSSS – significant difference between group with no change and mild to severe groupAdjusted FAB score did not differ significantly between groupsCaregiver burden. FBI-ALS disinhibition sub-score was significantly associated with CBI total score, developmental, physical, social and emotional burden sub-scoresFBI-ALS negative sub-score was significantly associated with developmental and physical burden sub-scoresAdjusted FAB score was associated with all sub-scores and total score of the FBI-ALSANCOVA analysis showed that patients with moderate to severe behavioral changes were associated with significantly higher caregiver burden in total CBI score as well as developmental and physical burden sub-scores Connection of bulbar palsy and behavior changes (frontal lobe involvement) suggested since patients with moderate to severe changes scored worse in bulbar functionIn contrast to many studies, apathy was not one of the major behavioral changes, but irritability, logopenia and inflexibility – no presence of pathogenic mutations (e.g. *C9orf72*) in Chinese population, so distinctive behavior changes in this population are suggestedDisease progression was not associated with behavioral impairment |
| Limitations | No information about caregiver genderNo assessment of QoL, depression or anxiety |

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### 1.2.5 Hsieh et al. (2016) – The evolution if caregiver burden in frontotemporal dementia with and without amyotrophic lateral sclerosis.

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| Reference | Hsieh, Sharpley; Leyton, Cristian E.; Caga, Jashelle; Flanagan, Emma; Kaizik, Cassandra; O'Connor, Claire M. et al. (2016): The Evolution of Caregiver Burden in Frontotemporal Dementia with and without Amyotrophic Lateral Sclerosis. In: *Journal of Alzheimer's disease : JAD* 49 (3), S. 875–885. DOI: 10.3233/JAD-150475. |
| Type | Controlled comparative study, descriptive study |
| Location/country | Sydney, Australia |
| Aim/subject | To assess and compare caregiver burden in bvFTD, semantic dementia (SD) and ALS-FTD |
| Participants | Recruitment from Frontier Frontotemporal Dementia Research Group and Forefront MND Clinic, Sydney, Australia; diagnosis confirmed by neurologist according to current diagnostic criteria, neurological and neurophysiological assessment, neuropsychological assessment and structural brain MRIALS patients: diagnosis of ALS according to El Escorial criteria and criteria for ALS-FTD, further classification according to initial FTD phenotype; total of 54 caregiver-patient dyads, 5 ALS-FTD patient drop-outs; median 2 or 3 follow-up visitsDiagnoses of patients: 8 ALS-FTD behavioral phenotype, 7 ALS-FTD language phenotype, 21 bvFTD, 18 SDAge of patients: ALS-FTD behavioral mean 63.3 years (±8.2), ALS-FTD language mean 62.7 (±4.6), bvFTD mean 63.6 (±9.5), SD mean 63.5 (±7.7)Gender of patients: not reportedEducation (years): ALS-FTD behavioral mean 12.2 (±3.9), ALS-FTD language mean 12.8 (±2.5), bvFTD mean 11.5 (±2.7), SD mean 12.31 (±3.6)Mean disease duration (months): ALS-FTD behavioral 46.9 (±32.6), ALS-FTD language 27.0 (±11.0), bvFTD 47.4 (±31.1), SD 51.6 (±24.7)Median number of follow-up visits: ALS-FTD behavioral 2 (IQR 1-2), ALS-FTD language 2 (IQR 1-3), bvFTD 3 (IQR 2-3), SD 3 (IQR 2-4)Age of caregiver: ALS-FTD (both phenotypes) mean 61.8 years (±8.7), bvFTD mean 56.2 (±10.3), SD mean 60.4 (±9.2)Gender of caregiver: ALS-FTD 7 male/8 female, bvFTD 2 male/19 female, SD 9 male/9 femaleRelationship to patient: ALS-FTD 14 spouses/1 other, bvFTD 16 spouses/5 other, SD 14 spouses/4 other |
| Methods/measures | Caregiver burden: assessed using the short Zarit Burden Interview (ZBI), score range 0-48, scores ≥17 indicating high burdenBehavioral changes: assessed using the Motor Neuron Disease Behavioral Scale (MiND-B), total score maximum 36, scores ≤33 indicating behavioral issues; three domains: apathy (max. 12, cutoff ≤8), disinhibition (max. 16, cutoff ≤12), stereotypical behavior (max. 8, cutoff ≤4)Cognitive functions: assessed using the Mini-Addenbrooke’s Cognitive Examination (M-ACE), maximum score 30, higher scores indicating better cognitive function, cutoff for suspected dementia ≤25, motor deficits were accounted for on the fluency domain  |
| Interventions | None |
| Outcomes | Baseline assessment – caregiver groups: mean level of burden was highest in bvFTD caregivers; ZBI rated as high in 76% of bvFTD, 47% of SD, and and 33% of ALS-FTD caregivers; baseline burden was not associated with caregiver gender or relationship to patient; baseline burden was associated with severity of neuropsychiatric symptoms in the SD and ALS-FTD groups, no associations between burden and M-ACE scores or disease durationBaseline assessment – patient groups: no differences between groups in M-ACE scores, neuropsychiatric symptoms rated highest in bvFTD patients, 100% of bvFTD patients below MiND-B cutoff (77% in SD patients, 93% in ALS-FTD patients); M-ACE and MiND-B scores were lower and in ALS-FTD behavioral phenotype cohort compared to language phenotype group; no differences in caregiver burden, caregiver age, patient age, or education between both ALS-FTD subgroups; no differences between demographic or clinical variables observed between limb-onset (n = 5) or bulbar-onset (n = 10) ALS-FTD patientsLongitudinal assessmentsCognitive scores: M-ACE scores tended to decline at the same rate in all three patient groups over time, although M-ACE scores themselves differed significantly; SD patients tended to obtain lower M-ACE scoresNeuropsychiatric symptoms: Severity of neuropsychiatric symptoms does not appear to change significantly over time, frequency of symptoms is greater in bvFTD patientsCaregiver burden: caregiver burden increased for SD and ALS-FTD groups over time but decreased, remaining at a high level, in the bvFTD group with a high baseline burdenPredictors of caregiver burden: Caregiver burden at the first follow-up was only predicted by baseline MiND-B ratings (accounting for 23% of the variance in burden at follow-up)SD caregivers might not expect behavioral changes since SD is treated as a language disorderEven though ALS-FTD patients have additional motor symptoms, caregiver burden is not as high as in bvFTD |
| Limitations | Small sample sizeDifferent follow-up timesNo control group (e.g. ALS patients without FTD)Some test items were hard to complete for motor impaired ALS patients |

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### 1.2.6 Lillo et al. (2012) – Caregiver burden in amyotrophic lateral sclerosis is more dependent on patients’ behavioral changes than physical disability.

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| Reference | Lillo, Patricia; Mioshi, Eneida; Hodges, John R. (2012): Caregiver burden in amyotrophic lateral sclerosis is more dependent on patients' behavioral changes than physical disability. A comparative study. In: *BMC neurology* 12, S. 156. DOI: 10.1186/1471-2377-12-156. |
| Type | Controlled cohort study, descriptive study |
| Location/country | Australia |
| Aim/subject | To assess the impact of behavioral changes and motor disability in ALS patients on caregiver burden and the frequency of depression, anxiety, and stress in ALS caregivers |
| Participants | Recruited via Motor Neuron Disease associations with an invitation to participate in a postal survey, 170 agreed to participate with 30 drop-outs 🡪 final number of usable responses n = 140 Age of patient: mean 63.5 years (±9)Disease duration: median 3 years (IQR 2-5)Region of onset: limb 73.6%, bulbar 26.4%ALSFRS-R total score (see below): mean 30.4 (±9.7)Age of caregiver: mean 60.8 years (±12)Gender of caregiver: 69.3% females Relationship to patient: 90% spouses, 7% children, 3% other |
| Methods/measures | Patient motor function: assessed using the self-administered form of the ALS Functional Rating Scale-Revised (ALSFRS-R) completed by patients and/or their caregivers, score range 0-48, a score of 48 denoting normal function, sub-scores bulbar, fine, gross and respiratory functionPatient behavioral changes: assessed using the Cambridge Behavioral Inventory-Revised (CBI-R) completed by caregivers, scores converted into percentages of impairment – 0-25% = mild, 26-50% = moderate, 51-75% = severe, >75% = very severeCaregiver depression, anxiety, and stress: assessed using the Depression, Anxiety and Stress Scale (DASS 21) completed by caregivers, subscale cut-off for depression >9, for anxiety >7, for stress >14, degree in all subscales divided into normal, mild, moderate, severe and extremely severeCaregiver burden: assessed using the short Zarit Burden Interview (ZBI) completed by caregivers, score range 0-48, a score ≥17 indicating high burden  |
| Interventions | None |
| Outcomes | Motor function: no significant difference between limb- and bulbar-onset groups in ALSFRS-R total score and respiratory function; limb-onset group having lower gross and fine motor function scores, bulbar-onset group having lower scores on bulbar functionBehavioral changes: abnormal behavior, stereotypical and motor behaviors and changes in eating habits reported in 50% of cases with 10-30% ranging in the moderate-severe category; apathy in 80% of cases with 40% showing moderate-severe apathy; no significant association between CBI-R scores and type of onsetDepression, anxiety, and stress: 69% of caregivers without significant depression, 23% showing moderate to very severe depression and 9% showing lesser degrees of depression; 16% of caregivers had moderate to extremely severe anxiety, 21% equivalent levels of stress; no association between DASS 21 sub-scores and type of onsetCaregiver burden: above cut-off ZBI scores reported by 48% of caregivers regardless of type of onset; regression model containing ALSFRS-R sub-scores, CBI-R domains mentioned above and DASS 21 sub-scores reached significance and explained 45-60% of variance in ZBI scores, significant predictors of high burden being abnormal behavior and stress, model classified 83.1% of caregivers with high burden correctlyIn comparison to pure FTD, caregiver depression had a lower impact on burden in ALS |
| Limitations | No information about patients who actually meet ALS-FTD criteriaSelection bias via the MND Association |

# Case reports

## 2.1 Chemali et al. (2010) – The plight of caring for young patients with frontotemporal dementia.

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| Reference | Chemali, Z.; Withall, A.; Daffner, K. R. (2010): The plight of caring for young patients with frontotemporal dementia. In: *American journal of Alzheimer's disease and other dementias* 25 (2), S. 109–115. DOI: 10.1177/1533317509352335. |
| Type | Case report |
| Location/country | USA |
| Aim/subject | To present the case of a 39-year-old individual with FTD and discuss challenges, obstacles and practical implications in caregiving with the results of a survey in a FTD caregiver support group |
| Participants | Patient SV, a 39-year-old female with FTDCost of Care survey:FTD Support Group in Boston – answered by 30 caregivers and family members who regularly attend the group  |
| Methods/measures | Case presentation about patient history, clinical examinations, hospital course and long-term treatmentCost of care survey  |
| Interventions | None |
| Outcomes | Case report:The patient was divorced and lost custody for her children following the onset of her symptoms – the patient was unemployed, lying about her financial situation, neglected her children and claimed she a had a boyfriend who in fact did not exist-, a similar disease history could be evaluated in the patient’s deceased mother, initial examinations in a neurology clinic did not lead to a diagnosis, the patient was arrested for fraud allegations, neither psychiatric nor neurological units accepted her, a friend found her sleeping under a bridge afterwardsA successful transferal to a tertiary psychiatric unit took place, FTD was confirmed as a diagnosis and a gene mutation was revealed, after 4 months, the patient was discharged and moved into a shelter home on antipsychotic medication, she is being provided with free care due to lack of health insurance and assisted in obtaining health care coverage through Medicaid Survey:53.3% patients were living at home, the majority being cared for by a sole caregiver or a part-time caregiver in addition to family care – 62.6% had a paid caregiver-, the majority of patients not living at home being admitted to a nursing home35.7% of patients living outside home had a monthly care cost of 5000$-9999$, 21.5% of patients required care costing more than 10 000$Implications for improvements in care for younger people with FTD are provided |
| Limitations | Small sample size in cost of care survey and lack of answersNo definition of what cost of compare comprises |

## 2.2 Kindell et al. (2014) – Living with semantic dementia. A case report of one family’s experience.

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| Reference | Kindell, Jacqueline; Sage, Karen; Wilkinson, Ray; Keady, John (2014): Living with semantic dementia. A Case report of one family's experience. In: *Qualitative health research* 24 (3), S. 401–411. DOI: 10.1177/1049732314521900. |
| Type | Case report |
| Location/country | United Kingdom |
| Aim/subject | To describe the caring situation of a wife and son caring for a patient with semantic dementia |
| Participants | Wife: 71 years, self-employed graphic designer still at work, length of marriage 45 yearsSon: lived close by, recently had lived with his parents while renovations were carried out in his housePatient: 71 years, retired lecturer of engineering, confirmed diagnosis of SD in 2006 (time of research: January 2011) |
| Methods/measures | 3 hours 20 minutes of semi-structured interview covering a range of concerns in caregiving for SD patients, undergoing narrative analysis: transcribed (107 pages) and coded for passages referring to specific incidents or issues by two coders Main themes of the caring experience were defined by consensus of both codersPrior to the interview, the interviewer developed an informal relationship to the interviewees by visiting the house on four extended visits, developing knowledge about their background and identity |
| Interventions | None  |
| Outcomes | Four recurring themes were identified:Living with routines: the patient developed various routines after onset of SD, e.g. regular trips to the local shop, preferred food, wearing the same clothes, watching the same TV programs; rubbing his hands on the soles of his shoes and various objects around the house, the latter being particularly disconcerting to the wife, talking about the same topicsPolicing and Protecting: wife and son had to keep the patient from doing certain chores and jobs around the house because he would create dangerous situations, he started to make ‘weird’ remarks and started swearing in public Making Connections: the patient rarely started a conversation and often would not engage much in topics proposed by his wife or son, the patient’s favorite topic often did not meet the interests of his wife or son, which made conversations difficult, patient used more hand gestures to communicateBeing adaptive and flexible: wife and son reported a personality change, i.e. the patient engaging in conversations with neighbors or strangers, e.g. walking their dogs or with children, even though he was a reserved person who did not like animals or children before; he now liked to watch different TV shows (entertainment shows instead of political programs), which the wife and son adapted toThe patient was happy within his routines, which made it necessary for the caregivers to adapt to it rather than being a chosen coping styleConstant vigilance regarding the patient’s action was mentally and physically challenging |
| Limitations | Selection bias |

## 2.3 Kumamoto et al. (2004) – Problems family caregivers encounter in home care of patients with frontotemporal lobar degeneration.

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| Reference | Kumamoto, Keigo; Arai, Yumiko; Hashimoto, Naoki; Ikeda, Manabu; Mizuno, Yutaka; Washio, Masakazu (2004): Problems family caregivers encounter in home care of patients with frontotemporal lobar degeneration. In: *Psychogeriatrics* 4 (2), S. 33–39. DOI: 10.1111/j.1479-8301.2004.00064.x. |
| Type | Case report |
| Location/country | Aichi prefecture, Japan |
| Aim/subject | To describe two cases of FTD and their caregiving. |
| Participants | Recruitment from an outpatient clinic in July 2002, two patients with FTD diagnosed according to Lund Manchester criteriaCase 1: 69-year-old female, 77-year-old husband as the primary caregiver; one daughter living outside the household; patient in day care 6 days/week since age 65; first symptoms at the age of 54, age of diagnosis not stated; CDR = 3, HDS-R = 0, Barthel index =6, PSMS = 0, IADL = 0; lost her job as a shop assistant as a result of her symptoms, dangerous driving, walks around the neighborhood and forces her way into neighbors’ homes, sings loudly and speaks and moves restlessly, forces large amounts of food into her mouth resulting in ingestion of food and making assisted feeding necessary, needs constant surveillance, cannot read; unpredictable behaviorCase 2: 69-year-old male, 62-year-old wife as the primary caregiver; one married son living nearby, daughter living further away; patient in day care 6 days/week; first symptoms at the age of 63, diagnosed at age 67; dangerous driving, when license was revoked he took long taxi rides that he couldn’t pay for; restless moving and repetitive shouting and singing; eats large amounts of food, needs complete assistance with grooming and is incontinent, random urination and defecation around the house; unpredictable behavior |
| Methods/measures | 2-hour semi-structured interviews with the caregiver only in a hospital consultation room, interview was not recorded according to caregiver preferences but notes were taken, patient course and problems in home caregiving were discussedDementia severity: assessed using the clinical dementia rating (CDR), administered by psychiatristCognitive function: assessed using the Hasegawa’s dementia scale (HDS-R), an equivalent to the Mini Mental State Examination used in JapanActivities of Daily Living (ADL) and instrumental ADL (IADL): assessed using the Barthel Index (20-point version), assessed using the physical self-maintenance scale (PSMS) and the IADL scale |
| Interventions | None |
| Outcomes | ADL: inappropriate food intake made bit-by-bit-feeding necessary in both cases to also avoid ingestion, dental problems resulted but were impossible to be treated due to reluctance of patients; patients were mobile and sometimes difficult to stop; grooming and bathing was entirely carried out by caregivers, being complicated by patients’ movement; defecation and urination often caused a significant amount of cleaning up because diapers were often leaking or being taken off by the patientBehavior and cognitive function: both patients underwent personality changes, initially presenting as ‘weary’ and ‘lacking energy’; patient 1 being later described as ‘puerile’ and the caregiver of patient 2 stating that she didn’t know what they were thinking about; patients were demanding and pleading while at the same time being resistant and violent towards the caregivers; also, ‘hitting’ the patient in those situations was reported; stereotypic and inappropriate behavior was present at all times and often lead to refusal in hospitals and other facilities; both patients were often roaming around, at first still finding their way back home, later only wandering around the neighborhood – this required constant vigilance of the caregivers; patients were, as reported by caregivers and day care staff, still to some extent able to understand what is being said to them and to perform certain activities, e.g. slicing vegetables in patient 1; no delusions or hallucinations reported |
| Limitations | Selection biasAssessment tool HDS-R equal to MMSE, which is questionable to detect cognitive changes in FTD (Piguet et al. 2013) |

## 2.4 Massimo et al. (2013) – Caring for loved ones with frontotemporal degeneration. The lived experiences of spouses.

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| Reference | Massimo, Lauren; Evans, Lois K.; Benner, Patricia (2013): Caring for loved ones with frontotemporal degeneration. The lived experiences of spouses. In: *Geriatric nursing (New York, N.Y.)* 34 (4), S. 302–306. DOI: 10.1016/j.gerinurse.2013.05.001. |
| Type | Case report  |
| Location/country | USA |
| Aim/subject | To portray the experiences of two wives providing care for a person with FTD |
| Participants | Wives of two FTD patients (age range mid-50s to early 60s), both spouses having FTD for less than two years and exhibiting behavioral symptoms |
| Methods/measures | 60-minute interviews conducted in the participant’s homes, general questions regarding the FTD diagnosis, difficulty of behaviors, difficulties as a caregiver, description of a good day framing the interviewAudio recording transcribed and entered into Atlas. ti 6 program, recurring themes identified and determined by consensus between two of the authors |
| Interventions | None |
| Outcomes | Identity and role change: spousal caregivers have to obtain new skills and specializations in their new role, the diagnosis was life-changing for both wives, roles as wife and husband were lost as well as shared memoriesIsolation: the wives were unable to talk about the situation to the patients because they lacked insight, this made the caregivers feel alienated and isolated with their feelings about the changing situationAnger: emotion most often described by both caregivers, they felt angry about socially inappropriate behavior, emotional coldness, lack of reciprocated feelings and experiencing the patient as ‘inconsiderate’Facing the future: caregivers had only vague ideas of a ‘perfect day’, e.g. doing nothing or also being very productive, but they also expressed hope for their husbands Reframing: Caregivers separated the disease from the person and adapted to reduced functioning in the patient, constantly reminding themselves of the pathology underlying the behavioral changes |
| Limitations | Selection bias |

## 2.5 Oyebode et al. (2013) – Relatives’ experiences of frontal-variant frontotemporal dementia.

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| Reference | Oyebode, Jan R.; Bradley, Paul; Allen, Joanne L. (2013): Relatives' experiences of frontal-variant frontotemporal dementia. In: *Qualitative health research* 23 (2), S. 156–166. DOI: 10.1177/1049732312466294. |
| Type | Case studies |
| Location/country | United Kingdom |
| Aim/subject | To highlight and explain different themes experienced in caregiving for a person with fvFTD by interviewing six caregivers. |
| Participants | Recruitment from two national specialized young-onset dementia centers, eligible family caregivers were approached and afterwards contacted by telephone to arrange the interviewInclusion criteria: family member, involved in care decisions; fluent in EnglishAll participants were first-degree relatives – three husbands, a wife, a daughter (all of them living with the patient) and a brother (patient living in residential care), all patients being diagnosed with fvFTD according to Lund Manchester criteria |
| Methods/measures | Semi-structured interview with the caregiver either in their own home or in the care home, respectively; one caregiver chose to have the care recipient present Mainly open questions were used, e.g. ‘Can you tell me about [the person with fvFTD] and your life now?’Interpretative phenomenological analysis (IPA) was used to analyse interview transcripts; excerpts of transcripts were discussed in group by authors, after rereading, initial motives were independently extracted, then again discussed; then, interpretative analyses identified themes for each transcript, partly joint and partly independently; finally, a set of master themes was derived from the findings of all interviews |
| Interventions | none |
| Outcomes | 11 themes were determined and sorted into 3 clusters: Witnessing bizarre and strange changes, Managing the Behaviors, Impact on the Relationship and the Person with fvFTD***Witnessing bizarre and strange changes****Changes in appetites and drives:* four patients were described to overeat, often sweet foods, or to walk excessively; in other patients, a lack of motivation was described, leading to problems with personal hygiene and the patients letting themselves go*Lack of forward planning:* patients were no longer able to plan forward or to complete complex tasks, leading some patients to lose their jobs; in two other cases, patients filled up their cars at petrol stations without being able to pay for it, another woman served raw food because she was unable to cook*Loss of inhibition leading to socially embarrassing behaviors:* all patients had undergone changes in behavior, such as voicing thoughts that usually would be kept to oneself, following urges in public or invading other people’s personal space; this behavior resulted in shoplifting, touching strangers, bizarre eating behavior*Risky behavior because of a lack of common sense and judgment:* loss of judgmental abilities led to injuries in 5 patients, e.g. burns incurred when trying to cook, risky behavior in traffic with damaging vehicles or riding the bicycle in the middle of traffic*Communication problems*: in four patients, communication abilities declined, often by reduced speech output, nonsense speech or difficulties to find the right words; loud chanting and shouting provoked other people’s reactions and was hard to understand or predict by caregivers***Managing the behaviors****Taking on tasks and roles:* co-residential caregivers took on a wide range of tasks and responsibilities, e.g. household chores, finances, driving, assisting and caring for the patient, sometimes along with their regular workplace; the brother of the patient living in residential care was the primary contact for care home staff, had organized the admission into the home and conveyed all the information to their elderly parents*Defending, asserting, and explaining*: caregivers needed to be assertive and persistent in finding appropriate support and services for the patients; caregivers sometimes explained uncommon behavior to others, also to avoid negative consequences for the patient; in two cases, even physically defense for the patient was necessary*Promoting quality of life:* five participants spoke about keeping the patient’s life stimulating, three participants used cognitive stimulation for that, three participants found walking helpful for the patients; four participants mentioned ‘safe havens’, non-judgmental environments where patients weren’t at risk of conflict due to their behavior, those havens could be the nursing home, a boat, a caravan or just the visit of a friend who accepted the patient the way they were*Working around a lack of awareness:* participants consistently reported that reasoning about behavior with the patient or using rational arguments was useless; instead, 2 participants said they tried to accept the patient’s behavior, 3 said they used white lies to keep patients from doing certain things, 3 said they reacted with humor to some behaviors to cope***Impact on the Relationship and the Person with fvFTD***All participants reported that the patient had undergone profound changes in their personality which was associated with sorrow and anticipatory grief as well as concerns of what the future might hold, one patient did rather express frustration than grief*Loss of the person and relationship, and heartbreak:* all patients were described not to be the same person anymore, despite being physically present; caregivers described the loss of affection to their partner or, reversely, the need of the patient for a sexual relationship despite being cared for most of the day by his wife; five participants described how they saw a bleak future coming up, being heartbroken about giving up on plans they had made before the disease*Sources of support, solace, and hope:* participants used both internal and external coping strategies, including formal support by professionals (5 participants), hope from participating in drug trials (4 participants), support from family (3 participants) or friends (2 participants, as well as living in the moment without looking back or into the future (2 participants) and a strategy not to blame the patient for their behavior, but the illness (2 participants); moreover, some patients reasoned that things could still be worse or experienced themselves to be stronger than they thought in the role as a caregiverIn comparison to AD, there was a lack of literature explicitly describing the most burdensome behaviors of AD patient, with suggestions of wandering, memory loss and repetitive questions being experienced as most burdensome, thus differing from the accounts interviewees gave on the socially embarrassing behavior fvFTD patients exhibit and lay stigma towards dementia diseasesAlso, there is a structural stigma, i.e. a lack of knowledge about the disease in healthcare professionals, leading to a lack of appropriate support services, making it necessary for the caregivers to be assertive and find tailored support |
| Limitations | Limited generalizability from small sample sizeNo conclusions could be drawn from age or relationship because of the mixed sampleSelection bias |

3 Interventions

## 3.1 Boxer et al. (2013) – Memantine in patients with frontotemporal lobar degeneration. A multicentre, randomised, double-blind, placebo-controlled trial.

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| Reference | Boxer, Adam L.; Knopman, David S.; Kaufer, Daniel I.; Grossman, Murray; Onyike, Chiadi; Graf-Radford, Neill et al. (2013): Memantine in patients with frontotemporal lobar degeneration. A multicentre, randomised, double-blind, placebo-controlled trial. In: *The Lancet Neurology* 12 (2), S. 149–156. DOI: 10.1016/S1474-4422(12)70320-4. |
| Type | RCT, double-blind placebo controlled |
| Location/country | USA |
| Aim/subject | To assess the efficacy of memantine treatment in FTD patients |
| Participants | Recruitment from nine memory clinics in the US, follow-up to a 26-week open-label study which included bvFTD and SD patients 🡪 bvFTD and SD cohort, no PNFA, inclusion of FTD-MND patients if motor impairments did not interfere with study proceduresInclusion criteria: age 40-80, MMSE ≥15, MRI confirming bvFTD or SD within 24 months before randomization to exclude bvFTD phenocopy cases, reliable caregiverExclusion criteria: PNFA, use of memantine, acetylcholinesterase inhibitors, lithium, valproate, antipsychotics, benzodiazepines in 4 weeks prior to randomization, presence of disorders precluding FTDUse of atypical antipsychotics allowed after baseline, use of antidepressants allowed if dose was stable at least 1 month prior to randomizationGroup distribution: 39 IG (memantine, 31 bvFTD, 8 SD), 42 CG (Placebo, 33 bvFTD, 9 SD)Age of patient (years): IG mean 65.8 (63.5-68.1 CI), CG mean 66.2 (63.8-68.6 CI)Gender of patient: IG 49% male, CG 76% maleEducation of patient (years): IG mean 15.7 (14.9-16.6 CI), CG mean 15.3 (14.5-16.2 CI)Disease duration (years): IG mean 3.0 (2.2-3.7 CI), CG mean 3.3 (2.6-4.1 CI)Weight (kg): IG mean 80.6 (74.9-86.3 CI), CG mean 86.2 (80-92.4 CI)Baseline characteristics; bvFTD and SD subcategory values reported |
| Methods/measures | *Randomization*Randomization using a random number generator, all patients and study personnel blinded to treatment*Primary outcomes*Neuropsychiatric Inventory (NPI)Clinical Global Impression of Change (CGIC)*Secondary outcomes*Clinical dementia rating sum of boxes (CDR-SB-FTD)Mini Mental State Examination (MMSE)Functional Activities Questionnaire (FAQ)Texas Functional Living Scale (TFLS)Executive interview (EXIT 25)Modified unified Parkinson’s disease rating scale (UPDRS)Time to initiation of antipsychotic therapyNeuropsychological battery containing a California verbal learning test, category fluency, phonemic fluency, Boston Naming Test (BNT), modified trails set-shifting task, backward digit span, digit symbol*Tertiary outcomes*Zarit Burden Interview (ZBI)Subject weight in kg (FTD patients often gain weight) |
| Interventions | *Intervention group (n=39, bvFTD n=31, SD n=8)*Baseline/randomization occurred within 35 days after screening visit, assessment of all outcome measures and initial administration of study medicationMemantine dose titrated by 5mg/week to a dose of 10mg memantine twice daily, orally takenStudy visits at 6, 12 and 26 weeks for safety and efficacy check-up; subset of outcomes measures assessed at weeks 6 and 12Phone call check-ups at 3, 9 and 18 weeksWeek 26: Ending of medication, assessment of all outcome measures30 days after ending: off-drug safety assessmentIn total 6 study visits over 35 weeks*Control group (n=42, bvFTD n=33, SD n=9)*Baseline/randomization occurred within 35 days after screening visit, assessment of all outcome measures and initial administration of study medicationPlacebo twice daily, taken orallyAll subsequent procedures equal to Intervention group  |
| Outcomes | In the IG, three patients discontinued treatment – two patients start excluded medications, one patient experienced an adverse eventIn the CG, two patients discontinued treatment, both experiencing adverse eventsSignificantly more men in the placebo groupStudy compliance 94.8% in the IG, 95.6% in the CGIntention-to-treat analysis: no significant difference in CGIC scores between IG and CGIG at week 26: 2 improved, 8 remained stable, 27 worsenedCG at week 26: 4 improved, 8 remained stable, 29 worsenedNo treatment effect on CDR-SB-FTD scores (increased similarly in both groups), FAQ and TFLS (similar decline in both groups)IG performed worse on BNT and digit symbol tests than CG, no differences in other neuropsychological testsMore cognitive adverse events in IG than CG, more psychiatric adverse events in CG than IGSerious adverse events (diverticulitis and vasovagal episode in CG, right-sided facial weakness and loss of consciousness in IG) not judged to be related to treatmentTime to use of antipsychotics not analyzed due to small number of applying participants (n=3)No effect on caregiver burden (ZBI) or weightTransient improvement of NPI in IG at week 6, but converged with CG at weeks 12 and 26BNT worse in both bvFTD and SD at week 26Digit symbol test performance increased slightly in CG, worsened in IGNo benefit of memantine treatment could be determined |
| Limitations | Age restrictionPlanned number of enrolments was not metNew, more sensitive FTD-specific behavior assessment tools were not in use when the study was designedNo information about caregiver characteristics (e.g. age, gender) availableUse of MMSE in FTD patients questionable (Piguet et al. 2013) |

## 3.2 Diehl et al. (2003): A support group for caregivers of patients with frontotemporal dementia.

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| Reference | Diehl, Janine; Mayer, T.; Förstl, H.; Kurz, A. (2003): A Support Group for Caregivers of Patients with Frontotemporal Dementia. In: *Dementia (London, England)* 2 (2), S. 151–161. DOI: 10.1177/1471301203002002002. |
| Type | Interventional study |
| Location/country | Germany |
| Aim/subject | To present findings from a support group for caregivers of FTD patients |
| Participants | 14 caregivers of FTD patients were addressed to participate in the support group, 8 accepted- all caregivers are female- age range: 46 to 69 years- 7 patients were diagnosed with FTD according to Lund Manchester criteria, 3 of them had SD/one patient with Binswanger’s disease with pronounced frontal symptoms- average disease duration: 7 years- patients from all severity stages- 7/8 patients were lower middle class, 7/8 living in the community- 4/8 families had adult children (not living with them), 3/8 spouses employed (1 in a part-time job) |
| Methods/measures | Participants were asked to evaluate the support group directly after the final session regarding their satisfaction with the program, Six months post intervention, participants were mailed a 14-item questionnaire with dichotomous yes/no statements regarding long-term effects of the group sessions (e.g. ‘The group has improved my understanding of the disease and of the patient’) |
| Interventions | 7 group sessions of 90 minutes duration with structured curriculum, moderated by a psychiatric and a neurologic resident: 1) Introduction, 2) Medical information, 3) problems at the early stages of the disease, 4) problems during progression, 5) Financial, legal and insurance issues (with a social worker), 6) How to get help, 7) visit to a nursing home for the mentally handicappedApart from educating the caregivers, the sessions also aimed to be therapeutic by exchanging personal experience, facilitating the expression of emotions, encourage participants in mutual support and to develop coping strategiesStructured sessions were followed by monthly self-help sessions which were not attended by moderators or professionals  |
| Outcomes | Education about FTD: emphasizing the fact that FTD is an organic brain disease is helpful for caregivers to accept the condition and to help develop realistic expectations of the future; social and legal advice was very much appreciated by caregiversSpecific problems and needs: offensive and egocentric behavior as well as lack of insight were most burdensome; caregivers found the support group to be helpful to deal with their emotions, especially the steady loss of a loved one, the feelings of embarrassment caused by the patient’s behavior, as well as feelings of guilt; some caregivers stated that there were positive aspects, such as a process of maturation, of caregivingMutual support and coping strategies: caregivers emphasized that it was useless to try to convince the patient that they have an illness, white lies and pretences were found to be more effective; open communication about and distancing oneself from the patient’s behavior can help with embarrassing situations and prevent social isolation; seeking psychological support was stated to be important; taking care of one’s own needs was emphasized and the group often was often the first occasion for the caregivers to do soProgram evaluation: understanding and knowledge were improved in all caregivers; three patients said they learned to take better care of their own needs; seven of eight participants continued to meet in an unmoderated support group, they found this to be very helpful; empathy and useful suggestions were provided; new social contacts and even friendships developed |
| Limitations | Pre-selected caregiver groupNo male caregiversComparison between AD and FTD caregiver burden not based on the same assessment toolsNo before/after comparison of caregiver burden |

## 3.3 Dowling et al. (2014) – Life enhancing activities for family caregivers of people with frontotemporal dementia.

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| Reference | Dowling, Glenna A.; Merrilees, Jennifer; Mastick, Judy; Chang, Vickie Y.; Hubbard, Erin; Moskowitz, Judith Tedlie (2014): Life enhancing activities for family caregivers of people with frontotemporal dementia. In: *Alzheimer disease and associated disorders* 28 (2), S. 175–181. DOI: 10.1097/WAD.0b013e3182a6b905. |
| Type | RCT |
| Location/country | USA |
| Aim/subject | To assess the feasibility of the positive affect intervention *Life Enhancing Activities for Family Caregivers* (LEAF) of people with FTD |
| Participants | Information about the study posted on University of California websites, the Association for Frontotemporal Degeneration Newsletter and support group communicationsInclusion criteria: primary care provider living with a family member with FTD, speak and read English, have Internet access that enables use of video communication, ability to provide informed consentExclusion criteria: severe cognitive impairment or active psychosis (assessed by interviewer)26 subjects enrolled between July 2011 and March 2012, 2 withdrawals before start 🡪 24 participants, 20 caregivers completing all sessions and follow-up assessmentsBaseline demographic data: Age of caregiver: skill group (skills) mean 59.42 years (±7.57), control group (control) mean 59.73 (±9.12)Gender of caregiver: 7 male/17 female; skills 25% male, control 36.4% maleYears of education: skills mean 17.25 (±2.05), control mean 16.27 (±2.15)Length of time as a caregiver: mean 4.2 years (±2.1, range 1-10)Ethnicity: 90% white, 10% Hispanic and African American |
| Methods/measures | For participants living in close proximity to UCSF campus, in-person sessions with the facilitator were offered, subjects living further away received sessions via video conference (VC), training call to assess technical details, care coverage for patient at the time of sessionRandomization of participants into skills or control group using a computer-generated random number sequenceBaseline interview before first session, first follow-up at week 6 (one week after completion of all sessions), second follow-up at week 10 (approximately one month after completion of all sessions), between-session homework, audio and video recording of the sessionsFacilitators who conducted the sessions were two specialist nurses for FTD and one psychologist, 1 participant took part in-person, all others were contacted via VCPositive and Negative Affect: assessed using a modified version of the Differential Emotions Scale (DES), positive and negative affects subscalesDepressive mood: assessed using the Center for Epidemiologic Studies Depression Scale (CES-D), 20 items rated on a 4-point scale according to frequency of experience during the previous weekCaregiver stress: assessed using the Perceived Stress Scale (PSS), score range 0-40, higher scores indicating greater stressCaregiver distress: assessed using the Neuropsychiatric Inventory (NPI): behavioral symptoms in patients and their effect on caregivers are rated by the caregiver, total score as a sum of each domain rating, score range 0-144, higher scores indicating higher distressCaregiver burden: assessed using the Zarit Burden Interview (ZBI)Evaluation questions: during sessions 2-6 participants were asked to rate previous week’s session and homework, final session included several Likert-type evaluation questions |
| Interventions | *Skills group:*12 participants were randomized to the LEAF intervention sessions, i.e. 5 sessions including skill-building in the area of positive affect and its influence as a coping strategy in caring for a person with FTDBaseline assessment of DES, CES-D, PSS, NPI and ZBISession 1: Positive Events and Gratitude (e.g. beginning a gratitude journal)Session 2: Mindfulness (e.g. meditation and breathing exercises)Session 3: Positive Reappraisal (e.g. reappraise negative or stressful occurrences)Session 4: Personal Strengths and Attainable Goal (e.g. define a goal and achieve it)Session 5: Altruistic Behaviors/Acts of Kindness – Doing for Others (e.g.doing something nice for somebody else every day)First follow-up at 6 weeks from baseline (DES, CES-D, PSS, NPI, ZBI)Second follow-up at 10 weeks from baseline*Control group:*12 participants were randomized to the control group, one-on-one sessions with the facilitator comparable in length to the intervention sessions (~1h), interview without didactic content or skills practice, completion of DES in each session, theme-centered questions to keep sessions different and interesting, daily affect reports as homeworkBaseline and follow-up assessment as in skills group |
| Outcomes | No significant demographic differences between groups, no difference between in-person participant and VC participantsPositive affect increased and negative effect (DES) decreased in intervention group compared to control group (CG); PSS and ZBI scores significantly improved in intervention group compared to CG; NPI scores improved compared to CG but did not reach significancePost-hoc pairwise interaction contrasts to assess between-group differences in each pair of weeks (e.g. week 1 vs. week 6)CES-D scores differed between groups at week 6 vs. week 10 – intervention group dropped below normative at-risk score for depression at week 10 (both groups at risk for clinical depression at baseline), NPI distress going down between weeks 6 and 10 in intervention group, CG showed slight increaseZBI scores decreased but remained moderate to severePositive effects of LEAF continued through week 10Control group perceived a nonsignificant increase in stress scoresSkills ranked most favorably were Positive events and gratitude, followed by goals, strength, positive reappraisal, kindness, mindfulness and capitalizingRecommendation of LEAF to others: range 0 (definitely not) to 10 (definitely yes) mean 9.64 (±0.67, range 8-10)Practice of skills: range 0 (not at all) to 4 (daily) mean 2.85 (±0.51, range 2.2-3.9)Using video communication: range 1 (very easy) to 5 (very difficult) mean 1.25 (±0.55, range 1-3)Video communication being the same as in-person interaction: range 1 (completely agree) to 5 (completely disagree) mean 2.35 (±1.09, range 1-5) |
| Limitations | Internet connection and as a limiting factor for accessibilityUtilization of VC program requires Internet literacy Lack of long-term follow-up although long-term effects are suggested |

## 3.4 Mioshi et al. (2013) – Improving burden and coping skills in frontotemporal dementia caregivers: a pilot study.

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| Reference | Mioshi, Eneida; McKinnon, Colleen; Savage, Sharon; O'Connor, Claire M.; Hodges, John R. (2013): Improving burden and coping skills in frontotemporal dementia caregivers: a pilot study. In: *Alzheimer disease and associated disorders* 27 (1), S. 84–86. DOI: 10.1097/WAD.0b013e31824a7f5b. |
| Type | Interventional study |
| Location/country | Sydney, Australia |
| Aim/subject | To explore the effects of a caregiver intervention addressing coping skills and cognitive appraisal for caregivers of FTD patients |
| Participants | Recruitment from Frontier FTD Research Clinic, of the identified 50 caregivers 21 agreed to participate, 12 caregivers were unable to attend intervention sessions and were therefore allocated in the control group (CG, see below), 🡪 9 in the intervention group (IG)Inclusion criteria: primary caregivers living in SydneyDementia severity and the patient living in a residential care facility did not lead to exclusionAge of patient: IG mean 64.4 years (±6.6), CG mean 66.8 (±9.6)Gender of patient: IG 100% male; CG 67% malePatients living at home: IG 89%, CG 92%Age of caregiver: IG mean 59 years (±5.9), CG mean 63 (±9.2)Gender of caregiver: IG 100% female, CG 67% femaleCaregivers currently in paid work: IG 56%, CG 34%Time providing care to the patient (h/week): IG 89.1 (±66), CG 113 (±69) |
| Methods/measures | Caregivers completed outcome measures via online survey*Primary outcome measures*Caregiver burden: assessed using the short Zarit Burden Interview (ZBI), scores >17 indicating significant burdenCaregivers’ reaction to patient behavioral problems: assessed using the Cambridge Behavioral Inventory-Revised (CBI-R), 5-point scale of how much behavior bothers caregivers *Secondary outcome measures*Psychological distress: assessed using the Depression, Anxiety, and Stress Scale (DASS 21), cut-off for depression ≥10, for anxiety ≥8 and for stress ≥15Coping skills: assessed using the COPE questionnaire that covers 15 dimensions of coping*Patient characteristics*Dementia severity: assessed using the Frontotemporal Dementia Rating Scale (FRS), stages: 5.39 to 4.12 = very mild; 3.35 to 1.92 = mild; 1.68 to -0.40 = moderate; -0.59 to -2.58 = severe, -3.09 to -4.99 = very severe, -4.98 to -6.66 = profoundBehavioral changes: assessed using the CBI-R (see above) |
| Interventions | *Intervention group* (n=9)Caregivers are trained in cognitive appraisal and coping strategies (problem solving, reframing, seeking support)Intervention sessions were held in a group format 2h/week for 15 weeks with two facilitatorsCompletion of online survey at baseline, after intervention (16 weeks), and at 12 months’ follow-up*Control group* (n=12)Completed only online survey at baseline and at an equivalent time after baseline according to the intervention group (16 weeks) |
| Outcomes | Greater proportion of male patients and female caregivers in the IG and a greater proportion of patients living at home in the CGZBI baseline scores were higher in the IG, but CBI-R scores were similarA significant decrease in caregiver burden and reaction to behaviors was observed in the IG while those remained unchanged in the CGLevels of burden and reactions to behaviors remained stable at 12 months in the IG when compared to 16 week’s follow-upNo changes in DASS 21 scoresOn the COPE questionnaire, there was a significant improvement in the sub-score ‘Humor’ |
| Limitations | No randomization Small sample sizeExclusively female caregivers in the IGDifferent baseline scores in IG and CG |

## 3.5 Moretti et al. (2004) – Rivastigmine in frontotemporal dementia: an open-label study.

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| Reference | Moretti, Rita; Torre, Paola; Antonello, Rodolfo M.; Cattaruzza, Tatiana; Cazzato, Giuseppe; Bava, Antonio (2004): Rivastigmine in frontotemporal dementia: an open-label study. In: *Drugs & aging* 21 (14), S. 931–937. |
| Type | Interventional study |
| Location/country | Trieste, Italy |
| Aim/subject | To examine the effects of rivastigmine, an acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) inhibitor in patients with FTD |
| Participants | Inclusion criteria: fulfilling criteria of the DSM-IV and the Lund and Manchester Criteria for probable FTDConfirmation of the diagnosis by MRIExclusion criteria: non-lacunar territorial infarcts, normal pressure hydrocephalus, cortical hemispheric large vessel strokes or lobar hemorrhages, history of significant head trauma, alcoholism, movement disorder, other conditions affecting frontal lobe function, tested impairment of semantic memory or linguistic patternManual division into intervention group (IG), n=20 and control group (CG), n=20Age of patient (years): IG mean 67.2 (±2.5), CG mean 68.3 (±1.4)Gender of patient: IG 11 male/9 female, CG 13 male/7 femaleDisease duration (months): IG mean 7.3 (±1.6), CG mean 6.9 (±0.75) |
| Methods/measures | *Behavioral and psychiatric symptoms of dementia (BPSD):*assessed using the Neuropsychiatric Inventory (NPI)assessed using the Cornell Scale for Depression in Dementia (CSDD)assessed using the Behavioral Pathology in Alzheimer’s Disease Rating Scale (BEHAVE-AD)*Caregiver stress*assessed using the Relative Stress Scale (RSS)*Clinical insight*assessed using the Clinical Insight Rating Scale (CIR)*Cognitive impairment*assessed using the Mini-Mental State Examination (MMSE)*Executive and planning functions*assessed using the Ten Point Clock Test (TPC)assessed using the Proverb Interpretation Tasks (PIT) |
| Interventions | *Intervention group (n=20)*received Rivastigmine 3 mg/day, titrated to 9 mg/day in 1.5 mg/day steps every 4 weekscompleted baseline and 12-month follow-up*Control group (n=20)*received the University of Trieste ‘standard’ treatment of FTD, i.e. drug treatment with antipsychotics, benzodiazepines and selegiline (deprenyl)completed baseline and 12-month follow-up*Both groups:* previous drug therapy was continued except for ACh receptor antagonists (one patient, discontinued 1 month before study entry); new prescription of psychoactive medication recorded over the study; treatment compliance assessed by caregivers |
| Outcomes | MRI scans showed clear frontal atrophy without asymmetric tendenciesBehavioral symptoms as measured with NPI and BEHAVE-AD significantly improved compared to baseline in the IG; NPI and BEHAVE-AD scores significantly worsened compared to baseline in the CGDeterioration of cognitive function as measured by the MMSE was not affected by rivastigmine treatmentIn the IG, 12 patients were taking antipsychotics or benzodiazepines at baseline compared to 8 at follow-up; this number increased in the CG but was not significantSide effects in the IG: 25% reported transitory nausea within the first 10 days of treatment, 20% reported muscle cramps within the first week, 15% reported blood pressure changes with a slight decrease of systolic pressureSide effects in the CG: 60% reported disequilibrium, 25% reported frequent falls, 35% reported nausea and dizziness throughout the time of treatmentRSS scores decreased significantly in the IG but not in the CGCSDD scores improved significantly in the CG but not in the IG |
| Limitations | No blinding, no randomizationSmall sample sizeOnly one follow-upNo information about caregiver characteristics (e.g. age, gender) availableUse of MMSE in FTD patients questionable (Piguet et al. 2013) |

## 3.6 O’Connell et al. (2014) – Development and evaluation of a telehealth videoconferenced support group for rural spouses of individuals diagnosed with atypical early-onset dementias.

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| Reference | O'Connell, Megan E.; Crossley, Margaret; Cammer, Allison; Morgan, Debra; Allingham, Wendy; Cheavins, Betty et al. (2014): Development and evaluation of a telehealth videoconferenced support group for rural spouses of individuals diagnosed with atypical early-onset dementias. In: *Dementia (London, England)* 13 (3), S. 382–395. DOI: 10.1177/1471301212474143. |
| Type | Interventional study |
| Location/country | Canada |
| Aim/subject | To develop a video-conferenced support group for caregivers of patient with atypical early-onset dementia and to evaluate its effectiveness |
| Participants | Spousal caregivers of patients with a disease from the FTD spectrum living in Saskatchewan, recruited from Rural and Remote Memory Clinic (RRMC)10 of originally 11 participants continued throughout the time of interventionPatients’ diagnoses: 1 PNFA, 3 SD, 4 bvFTD, 1 secondary dementia due to Huntington’s disease, 1 after multiple strokes affecting the frontal lobeSpouses were mostly in their 40s and 50s, one spouse was 83 years old at the beginning of the intervention; time since diagnosis ranged from some months to three years, all patients living at home at beginning |
| Methods/measures | High attendance and low attrition ratesOngoing attendance even after spouse’s death In-person workshop 18 months after inception of the group – discussions were recorded, transcribed and thematically analyzedDiscussion of these empirical themes at three years post-inceptionFacilitators documented their impressions |
| Interventions | Monthly 90-minute videoconference support group initiated in 2009, participants travelled to Saskatchewan telehealth sites (in hospitals) to use the equipment and high-speed internet connectionCaregivers agreed to focus on emotion-processing rather than psychoeducation in the group and kept an open agenda with a brief check-in in which every caregiver could describe their current situation and problems at the beginning of each sessionPsychologist co-facilitators moderated the group and provided expertise in special questions |
| Outcomes | 7 of 10 caregivers experienced their spouses entering long-term care6 patients had deceased at the time the article was writtenCaregivers rated as helpful the fact that all participants were caring for a spouse with an FTD disease, clearly noting the difference to AD caregivingMostly similar age was regarded as an advantage, also the fact that all caregivers were spouses because fundamental changes in the marital relationship, including sexuality, could be discussed openlyHeterogeneity was appreciated in the way that different stages of the disease could be discussed, equipping caregivers with ideas of what to expect from the futureCaregivers felt that 10 participants were the highest feasible number for the videoconference format, they appreciated the open frame and the possibility to discontinue at the point of choice; sharing their needs and experiences was very important for caregiversSocial contact and peer information including practical tips regarding finances, social security etc. could be exchanged, altruism developed with some group members eventually being advocates for FTD researchAspects for improvement: extending the group beyond families seen at the RRMC, technical difficulties, some caregivers had a lengthy travel to the next Telehealth center (up to 60 km); lack of interpersonal connections creating some distance, e.g. when requesting help; extra-group communications with formation of subgroups of caregivers living in the same community (solved by openly talking about it) |
| Limitations | No objective measures of efficacy (e.g. burden), no control group |

## 3.7 O’Connor et al. (2016) – Enhancing caregivers’ understanding of dementia and tailoring activities in frontotemporal dementia. Two case studies.

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| Reference | O'Connor, Claire M.; Clemson, Lindy; Brodaty, Henry; Gitlin, Laura N.; Piguet, Olivier; Mioshi, Eneida (2016): Enhancing caregivers' understanding of dementia and tailoring activities in frontotemporal dementia. Two case studies. In: *Disability and rehabilitation* 38 (7), S. 704–714. DOI: 10.3109/09638288.2015.1055375. |
| Type | Case report/caregiver intervention |
| Location/country | Australia |
| Aim/subject | To describe the Tailored Activities Program (TAP) intervention in two persons with FTD |
| Participants | Two cases of a cohort from an RCT examining the efficacy of TAPCase 1: Mrs V., 51 years, female, retired due to bvFTD, 18 months of symptoms prior to diagnosis in 2013, primary caregiver: husband, 53 years, two children (20 and 17) living in the same household and assisting with care, no comorbidities, urinary incontinence, dementia rated as severe on the FRSCase 2: Mr W., 62 years, male, retired 3 years after diagnosis of right-sided svPPA in 2003, symptom onset 2 years before diagnosis; primary caregiver: 26-year-old daughter (second youngest of five children) who had recently completed a Masters Degree in Dementia care; wife working full-time; SSRI medication for depression, dementia rated as severe on the FRS |
| Methods/measures | Assessment and baseline and 4 months after completion of the interventionFunctional cognition: assessment described in ‘Intervention’, see belowBehavioral symptoms: assessed using the NPI-C Functional deficits: assessed using the Disability Assessment for Dementia (DAD), measuring instrumental (IADLs) and basic activities of daily living (BADLs)General cognition: assessed using the Montreal Cognitive Assessment (MoCA), maximum score 30, higher scores indicating better cognitive functioningDisease severity: assessed using the Frontotemporal Dementia Rating Scale (FRS) via caregiver interview, yields six severity stages from very mild to profoundCaregiver confidence in using activities: assessed using an amended version of the original confidence scale from the TAP pilot study, 8 items rated from 0-10Caregiver vigilance/time spent caring: assessed using the Caregiver Vigilance Scale, estimate of time spent ‘doing things’ and ‘being there’ facets of caring |
| Interventions | Implemented as in the Australian TAP randomized controlled trial protocol, ethical approval obtained;Patients receive eight occupational therapy home visits with a length of 60 to 90 mins over a 4-month periodThree phases:1) assessment of patient and their environment via caregiver interview; assessment of patient’s functional cognition using the Large Allen Cognitive Level Screen (LACLS) and Allen’s Diagnostic Module (ADM) placemat task 2) introduction of tailored activities with the patient and their caregiver3) closure with education of the caregiver about generalization of learned strategies for the futureThree activities are identified for each patient based in their interests and habit, then tailored to their current abilities; therapist writes description of abilities, activity goals and specific directions for the caregiver; amended version of the TAP caregiver manual for FTD is handed to the caregivers |
| Outcomes | Mrs V presented motor disturbance (restlessness), disinhibition, apathy and elation/euphoria; the caregiver learned to motivate her for activities with an immediate outcome (e.g. preparing lunch for herself and eating it), would consider timing (e.g. days and daytimes with increased fatigue), allow more time to do a task, set up activities before prompting her to engage in it, change expectations for activities, relax rules and set up consistent routines – activities were watching DVDs/playing Wii Sports, assisting with meal preparation, feeding the dogCognitive performance declined while ADL performance improved, five out of eight behaviors recorded on the NPI-C were no longer present, caregiver distress declined, the caregiver spent slightly more time ‘doing something’ but felt less time ‘being on duty’, his confidence increasedMr W presented rigid behavior, rigid routines, clockwatching and would react agitated aggressively if being disturbed in these activities; this complicated assessment and eventually led to his daughter introducing all activities because he was suspicious of the therapist; the caregiver learned to carefully introduce new activities patiently and in a way the patient feels compelled to complete the activity, offering activities that meet the rigid routine behavior of the patient and his strengths, e.g. addressing his former work as an electrician, except for delusions and dysphoria, all other behavioral symptoms produced similar or lower levels of caregiver distress compared to baseline, vigilance times but also confidence declined at follow-up |
| Limitations | Selection biasLimited generalizability |

## 3.8 Vercelletto et al. (2011) – Memantine in behavioral variant frontotemporal dementia. Negative results.

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| Reference | Vercelletto, Martine; Boutoleau-Bretonnière, Claire; Volteau, Christelle; Puel, Michèle; Auriacombe, Sophie; Sarazin, Marie et al. (2011): Memantine in behavioral variant frontotemporal dementia. Negative results. In: *Journal of Alzheimer's disease : JAD* 23 (4), S. 749–759. DOI: 10.3233/JAD-2010-101632. |
| Type | RCT, DBPC |
| Location/country | France |
| Aim/subject | To test the efficacy and tolerability of memantine, an antagonist of NMDA ionotropic glutamate receptors, in bvFTD patients. |
| Participants | Recruitment from multiple centers in France between September 2006 and June 2008; inclusion criteria: bvFTD diagnosis according to Neary criteria for at least one year, age between 45 to 75 years, MMSE score ≥19, Frontotemporal Behavioral Scale >3, MADRS score <20, psychotropic medication allowed if stable for 3 months, reliable caregiver;exclusion criteria: SD or PNFA diagnosis, MND involvement, patients treated with acetylcholinesterase inhibitorsGroup allocation: 23 IG, 26 CGAge of patient (years): Intervention Group (IG) mean 64.4 (±7.5), Control Group (CG) 66.6 (±7.4)Gender of patient: IG 65.2% male, CG 61.5% maleDuration of symptoms (years): IG mean 4.3 (±2.8), CG mean 4.7 (±3.6)All patients were Caucasian. |
| Methods/measures | *Procedure*Random allocation into groups, identical packaging for placebo and memantine, participants and study personnel blinded to treatment*Assessment*Primary endpoint: assessed using the Clinician’s Interview-based Impression of Severity (CIBIS), assessing the condition and functioning on a 7-point scale; also assessing the change in comparison to baseline (CIBIC-Plus), assessed in a semi-structured interview with patient and caregiverSecondary endpoints:Behavior: assessed using the Neuropsychiatric Inventory (NPI), assessed using the Frontal Behavioral Inventory (FBI)Cognition: assessed using the Mini Mental State Exam (MMSE), assessed using the Mattis Dementia Rating Scale (MDRS)AdL: assessed using the Disability Assessment Daily (DAD)Caregiver burden: assessed using the Zarit Burden Interview (ZBI)Statistical analysis: analysis based on intention-to-treat (ITT) population (all patients who receives at least one dose and one assessment) |
| Interventions | *Intervention group (n = 23)*patients received 10 mg memantine, titrated gradually during the first three weeks,Screening 21-7 days before randomization, Randomization = M0, one visit per month during the first three months, then one visit every three months; CIBIC-Plus and all secondary endpoints assessed at M3, M6, M9 and M12; adverse effects recorded at every visit, set of physical examination incl. blood analysis at inclusion, M3 and M124 drop-outs 🡪 n = 19 at endpoint*Placebo group/control group (n = 26)*Patients received placebo twice daily, all other procedures similar to intervention group3 drop-outs 🡪 n = 23 at endpoint |
| Outcomes | CIBIC-Plus data at endpoint did not differ significantly between IG and CGThere was no significant difference in secondary endpoint data, only the FBI score increased more quickly in the CGNo significant differences in laboratory parametersAdverse effects reported in both groups, no treatment withdrawals due to adverse effects |
| Limitations | Small sample sizeTreatment duration could not be extended due to expiry of drugsInclusion of mild cases onlyNo information about caregiver characteristics (e.g. age, gender) availableUse of MMSE in FTD patients questionable (Piguet et al. 2013) |

# 4 Educational articles and reviews

## 4.1 Caceres et al. (2016) – Family caregivers of patients with frontotemporal dementia. An integrative review.

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| Reference | Caceres, Billy A.; Frank, Mayu O.; Jun, Jin; Martelly, Melissa T.; Sadarangani, Tina; Sales, Paloma Cesar de (2016): Family caregivers of patients with frontotemporal dementia. An integrative review. In: *International journal of nursing studies* 55, S. 71–84. DOI: 10.1016/j.ijnurstu.2015.10.016. |
| Type | Integrative review |
| Location/country | United States |
| Aim/subject | To identify characteristics of family caregivers of patients with FTD, assess the impact of caregiving for FTD patients on caregiver health and well-being, identify coping strategies uses by FTD family caregivers, evaluate the experience of family caregivers of FTD patients |
| Participants | N/a |
| Methods/measures | Search strategy: key words and combinations were “frontotemporal dementia”, “caregiver”, “family”, “frontotemporal dementia AND caregiver”, “frontotemporal dementia AND family”Databases used were PubMed/Medline, Embase, CINAHL, Web of ScienceInclusion criteria: English language, published in peer-reviewed journals, published between 1984 and 2015Exclusion criteria: <80% family members, focusing on FTD patients in institutional settings, interventional or case studies (focus on informal caregiving), non-primary settings (incl. review articles), publications including Alzheimer’s disease or other types of dementia, unpublished manuscripts or dissertations Data evaluation: Crowe Critical Appraisal Tool (CCAT) used by two independent reviewers to critique each article, if subject of article was found not to be worth considering it was excluded from the review, third reviewer would have been consulted in case of disagreementData analysis: data reduction – extraction of similar data from all articles, data display – organizing data to facilitate comparison, data comparison – patterns and relationships identified, conclusion drawing – identification of commonalities and differences, verification – confirmation of conclusions |
| Interventions | N/a |
| Outcomes | Search results: final sample consisting of eight quantitative and three qualitative articles representing eight study cohortsQuality appraisal: seven articles rated strong with scores 33-37 out of 40, four articles with scores from 19.5-26 out of 40 but did not meet exclusion criteriaAll articles provided information about family caregivers, coping strategies and overall impact of caregivingCaregiver and patient characteristics: average age of patient: 64-67 yearsaverage age of caregivers: 58-62 yearswomen more likely to be caregivers and made up more than 64% in most articlesmost caregivers were spouses and younger than the patient, some articles reported about children and sibling caregiversone article reported race/ethnicity, mainly White caregivers and patientsCaregiving impact on health and well-being: all but one studies used validated tools to measure mental and/or physical health, one relied on self-report; predisposition for depressive symptoms were found in spousal caregivers, deteriorated patient-caregiver relationship, caring for male FTD patients; caregiver reactions following the FTD diagnosis were mostly negative; negative emotion was predicted by frequency of behavioral disturbance, caregiver strain was associated with loss of insight and loss of motivation as measured by the NPI, apathy and communication difficulties were identified as challenging; Mental Component Summary (assessing mental health) in caregivers was decreased in caregivers experiencing strain and associated with worse scores on the Frontal Behavioral Inventory in patientsFavorable behaviors for caregiver mental health included increased appetite and sleepCaregiver distress is mainly based on apathy, isolation and alienation, uncertainty about the futurePhysical health was discussed less often, two studies used the Physical Component Summary: increased age, patient’s behavioral symptoms and caring for a male patient worsened physical health, better scores were observed in caregivers who used problem-oriented coping rather than emotion-oriented coping strategiesOne study examined perceived control in caregivers, high perceived control increased mental, but not physical well-beingCoping strategies: caregiver-developed strategies included humor and the use of “white lies” to neutralize disruptive behavior and were considered beneficialMostly females employed both problem-focused and emotion-focused coping strategies; dysfunctional coping strategies were mostly observed in higher age of caregivers – coping measuring scales however had low internal consistencySupport strategies suggested were information, social support including financial support, support from family members, friends and healthcare providersParticipating in hobbies outside of the home and education of others about behavioral disturbances were identified as beneficial coping strategiesAn online group was found helpful for children of FTD patients aged 11-18Reminiscing about positive memories, coming to terms with the unalterable change in the relationship to the patient and adapting to the role as a caregiver were found to be important in the process of acceptanceBoth children and adults could use the attribution of disruptive behavior to the condition instead of the individual as a helpful coping strategySamples consisted of mainly female caregivers, screening of studies suggests that female FTD patients are more likely to be institutionalizedSpousal caregivers experience greater burden than children, the latter however face different challengesCaregivers should be provided with education about FTD and its symptoms, access to support groups, access to coordinated care, strategies for managing behavioral disturbances and coping strategies, this requires sufficient knowledge about FTD in professional healthcare providers |
| Limitations | Publication biasLanguage biasSelection bias excluding articles that include other types of dementia and interventional or case studies |

## 4.2 Diehl et al. (2004) – Frontotemporale Demenz. Besondere Probleme für die Angehörigen.

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| Reference | Diehl, Janine; Forstl, H.; Jansen, S.; Kurz, A. (2004): Frontotemporale Demenz. Besondere Probleme fur die Angehorigen. In: *Zeitschrift fur Gerontologie und Geriatrie* 37 (4), S. 301–306. DOI: 10.1007/s00391-004-0202-9. (ARTICLE IN GERMAN) |
| Type | Educational article |
| Location/country | Munich, Germany |
| Aim/subject | To review clinical characteristics of FTD, to outline special problems caregivers are confronted with and to describe novel caregiver interventions |
| Participants | n/a |
| Methods/measures | Not reported |
| Interventions | None |
| Outcomes | Low prevalence of FTD leads to lack of knowledge in health care professionals and difficulties in finding other caregivers with similar experiencesEarly age of onset often hits patients when they are still working and/or have underage children living at home to care forBehavioral change is often misinterpreted and leads to difficulties in obtaining the right diagnosis; behavioral problems cause conflicts in families and may lead to institutionalization, which is often problematic because people cared for in nursing facilities are often much olderIn the USA, the UK and Sweden, associations for FTD have been established that also provide education about the condition, also using telephone and internet services; health care professionals should be educated about FTD |
| Limitations | No systematic literature selection |

## 4.3 Houseman et al. (2013) – Frontotemporal degeneration in the patient with amyotrophic lateral sclerosis. Helping the caregiver cope.

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| Reference | Houseman, Gail; Walsh, Susan; Brothers, Allyson; Lyter, Judy; Simmons, Zachary; Klapper, Jennifer (2013): Frontotemporal degeneration in the patient with amyotrophic lateral sclerosis. Helping the caregiver cope. In: *The Journal of neuroscience nursing : journal of the American Association of Neuroscience Nurses* 45 (2), S. 96–100. DOI: 10.1097/JNN.0b013e318282900b. |
| Type | Educational article |
| Location/country | Pennsylvania, USA |
| Aim/subject | To provide information about nursing care for patients with ALS-FTD and outline interventions |
| Participants | n/a |
| Methods/measures | Literature review (PubMed, Medline, Cochrane Library of Evidence-Based ReviewsExpert opinion from ALS cliniciansALS-FTD caregiver interviews (part of a related study) |
| Interventions | Theoretically outlined (see below) |
| Outcomes | Nurses should provide education about the disease so that caregivers can understand patients’ behavior and to clarify the difference between AD and FTDNurses should make sure safety and environmental issues are addressed, e.g. medication management, driving, financial resources, use of power tools, keeping potentially dangerous objects (firearms, unsafe foods) away from the patientNurses can assist caregivers in determining patterns of patient’s behavior and its managementNurses can support patients and caregivers in decision-making, concerning medical treatment and power of attorney |
| Limitations | No description of literature search strategyPresented interventions not evidence-based |

## 4.4 LoGiudice and Hassett (2005) – Uncommon dementia and the carer’s perspective.

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| Reference | LoGiudice, D.; Hassett, A. (2005): Uncommon dementia and the carer's perspective. In: *International psychogeriatrics* 17 (S1), S223. DOI: 10.1017/S1041610205002048. |
| Type | Educational article |
| Location/country | Australia |
| Aim/subject | To highlight special features in caregiving for people with uncommon dementia, i.e. FTD, Huntington’s disease (HD) and dementia related to HIV |
| Participants | n/a |
| Methods/measures | Not reported |
| Interventions | None |
| Outcomes | Atypical dementias usually have their onset during middle or even young adulthood, meaning the patient cannot further fulfil his role as a provider, caregivers have to face financial issues (e.g. children financially dependent) as well as the increasing dependency of the patient in daily living; families become frustrated by the patient’s behavior and can also be traumatized, especially when diagnosis and thus an explanation for the inappropriateness is delayed – at the actual time of diagnosis, caregivers face a radical change as being thrust into their new roleCharacteristics: research mainly reports about wives and adult children, lack of information about husbands, adolescents and younger children in the families – caregivers are usually younger and thus less physically impaired compared to older dementia caregivers, but their new role does not align with age-typical requirements and expectations; positively, adolescents may experience stronger familial cohesionFTD: lack of knowledge about the disease, financial problems (also caused by inappropriate spending and altercations with the law) are specifically burdening, little is known about interventions both for caregivers and patients, e.g. behavior-modifying drugsDifficulties in caregiving about Huntington’s disease and HIV-related dementia providedProblems should be addressed in a multidisciplinary team approach and flexible and reliable support should be provided to make caregivers of atypical dementia patients feel understood |
| Limitations | No selection strategy for reviewed literature providedEvidence of presented data questionable |

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## 4.5 Massimo and Evans (2014) – Differentiating subtypes of apathy to improve person-centered care in frontotemporal degeneration.

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| Reference | Massimo, Lauren; Evans, Lois K. (2014): Differentiating subtypes of apathy to improve person-centered care in frontotemporal degeneration. In: *Journal of gerontological nursing* 40 (10), S. 58–65. DOI: 10.3928/00989134-20140827-01. |
| Type | Educational article |
| Location/country | USA |
| Aim/subject | To differentiate three types of apathy and to establish their implications on person-centered care in Frontotemporal Degeneration  |
| Participants | n/a |
| Methods/measures | Not reported |
| Interventions | None |
| Outcomes | Model of apathy as a lack of goal-directed behavior (GDB) is described – apathy can occur in the1) initiation of an action2) the planning of an action3) the motivation for an actionThe Philadelphia Apathy Computerized Test (PACT) is presented to measure and quantify components of apathy that are not assessed by e.g. the NPINurses should assess the subtype of apathy in order to be able to provide effective interventions, e.g. multisensory stimulation for patients with initiation difficulties, restructuring complex activities into simpler components for planning difficulties, increasing rewards for motivation difficultiesApathy is often being overlooked because there is no apparent distress and often assessed by proxy report |
| Limitations | No information about evidence of presented concepts available |

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## 4.6 McCarter et al. (2016) – Sleep disturbances in frontotemporal dementia.

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| Reference | McCarter, Stuart J.; St Louis, Erik K.; Boeve, Bradley F. (2016): Sleep Disturbances in Frontotemporal Dementia. In: *Current neurology and neuroscience reports* 16 (9), S. 85. DOI: 10.1007/s11910-016-0680-3. |
| Type | Review |
| Location/country | USA |
| Aim/subject | To describe sleep disturbances and possible treatment options in FTD |
| Participants | n/a |
| Methods/measures | Not reported |
| Interventions | none |
| Outcomes | 33 to 76% of FTD patients are estimated to have sleep or night time behavioral disturbances, more PPA patients seem to be affected compared to bvFTD The most common identified disturbances are- Sleep disordered breathing (SDB), i.e. apnea during sleep (present in ~68%- Insomnia (present in ~ 48%)- Excessive daytime sleepiness (EDS, present in ~64%)- Restless legs syndrome (RLS, present in ~8%)- REM sleep behavior disorder, i.e. loss of skeletal muscle atonia during REM sleep with an increased risk for injuries, rarely presentTreatment options are presented for each disturbanceNo treatment guidelines for sleep disturbances published at time of publication, physicians should assess four major symptom complexes (insomnia, hypersomnia, excessive motor activity at night, nocturnal hallucinations/behavioral problems) in an interview featuring both patient and caregiver reportsSleep disturbances contribute significantly to caregiver burden |
| Limitations | No information on literature search strategy |

## 4.7 Merrilees (2007) – A model for management of behavioral symptoms in frontotemporal lobar degeneration.

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| Reference | Merrilees, Jennifer (2007): A model for management of behavioral symptoms in frontotemporal lobar degeneration. In: *Alzheimer disease and associated disorders* 21 (4), S64-9. DOI: 10.1097/WAD.0b013e31815bf774. |
| Type | Educational article |
| Location/country | USA |
| Aim/subject | To describe a model for managing behavioral symptoms that occur in FTLD |
| Participants | n/a |
| Methods/measures | Description of the A(ntecedent)-B(ehavior)-C(onsequence)-Model in four case vignettes and examples of FTD patients from clinical practice |
| Interventions | Suggested use of the ABC-model (see below) |
| Outcomes | ABC-Model: Antecedent, i.e. a trigger or a cause for problematic behaviors, in the case of FTD the atrophy of frontal lobe tissue, also environmental triggers that might upset the patientBehavior, i.e. the disturbing behavior that occurs Consequence, i.e. the way caregivers respond to the problematic behaviorFTLD characteristics and underlying brain atrophy regions are describedCase 1 – a disinhibited patient who stands uncomfortably close to others, talks inappropriately to strangers, takes food from other plates, A – frontal lobe atrophy; B – disinhibition that is embarrassing for caregivers; C – brief explanation of the behavior for others using a business card format, distracting the patient, limiting contact to the public, possible use of a SSRI Case 2 – a patient that follows strict routines, e.g. playing the same computer game, following a time consuming personal hygiene routine, A - right temporal lobe atrophy; B – habits and rituals; C – accept the behavior, in this case encourage the patient to play the game on a portable device so they can leave the houseCase 3 – a patient that exhibits apathy, caregivers feel he might be bored or depressed, A – frontal lobe atrophy; B – apathy, C – acceptance of the behavior, engaging in more passive activities, e.g. watching television togetherCase 4 – a patient that is aggressive when being restricted from driving his car although his driving license was revoked, there were weapons in the house A – frontal lobe atrophy, his family members driving the patient’s car; B – aggression; C – staying physically clear of the patient, family stopped driving the car, the car was disabled but the patient was given the car keys to carry, weapons were removed, an SSRI was usedBehavior can further be modified by substitution of disruptive behavior by more acceptable alternatives (e.g. a former physician acted intrusive in his nursing home, but stopped after he was allowed to take his nurses’ blood pressure)Medical evaluation should be sought to rule out other antecedents of the behavior – e.g. changed toilet habits could be caused by an infectionEnvironmental modification for the patients up to physical restriction, e.g. locking doors, could be used as well as pharmacological treatment to dampen behavioral symptoms |
| Limitations | Based on clinical practice experience, but no controlled trial |

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## 4.8 Morhardt (2011) – Accessing community-based and long-term care services. Challenges facing persons with frontotemporal dementia and their families.

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| Reference | Morhardt, Darby (2011): Accessing community-based and long-term care services. Challenges facing persons with frontotemporal dementia and their families. In: *Journal of molecular neuroscience : MN* 45 (3), S. 737–741. DOI: 10.1007/s12031-011-9612-5. |
| Type | Educational article |
| Location/country | USA |
| Aim/subject | To outline challenges of caregivers and patients accessing care services |
| Participants | n/a |
| Methods/measures | Experiences from 15 years of clinical social work with FTD patients and caregivers |
| Interventions | None |
| Outcomes | Four main problems were reported:1) Difficulty obtaining a diagnosis: early symptoms are often misinterpreted for personality disorders, depression, psychosis etc. because many physicians do not consider the possibility of a neurodegenerative disease, deterioration of familial relationships may even lead to divorce2) Financial concerns: FTD patients often cannot fulfil the demands of their workplace which may lead to conflict and even loss of their job, while often being at the height of their careers at onset; excessive spending or poor financial management as a result of the condition may further worsen the financial situation for the family3) Social Security Disability and Medicare 2-year wait: the situation in the US in 2011 is described here, Social Security Disability Insurance (SSDI) benefits are now available faster, still patients have to face a 2-year waiting time until they can receive Medicare health insurance after the benefits have been approved, this puts additional financial pressure and either living with no insurance or partial coverage for this time; however, a health reform is supposed to end this waiting time4) Community services: lack of services for dementia patients younger than 60, lack of knowledge in health care professionals, many care facilities reject FTD patients because they are unable to manage behavioral symptoms or would need more staff to do so, FTD patients are different to the structure of often elderly AD patients in care facilities; however, few successful care programs with a multidisciplinary approach do exist; the ABC-model as described by Merrilees (2007) is presented |
| Limitations | Presented content based on clinical experience, no controlled validation |

## 4.9 Nunnemann et al. (2012) – Caregivers of patients with frontotemporal lobar degeneration. A review of burden, problems, needs and interventions.

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| Reference | Nunnemann, Sabine; Kurz, Alexander; Leucht, Stefan; Diehl-Schmid, Janine (2012): Caregivers of patients with frontotemporal lobar degeneration. A review of burden, problems, needs, and interventions. In: *International psychogeriatrics* 24 (9), S. 1368–1386. DOI: 10.1017/S104161021200035X. |
| Type | Systematic review |
| Location/country | Munich, Germany |
| Aim/subject | To outline burden and problems in FTLD caregivers and possible interventions. |
| Participants | n/a |
| Methods/measures | Systematic review using Medline, CINAHL, Embase, Cochrane Library: Cochrane Dementia and Cognitive Improvement Group, Psyndex, PsycINFO, SocINDEX, SOWIPORT, WISO, Social Sciences Citation Index, Periodicals Index Online up to May 2011; 6th (2008) and 7th (2010) International Conferences on Frontotemporal Dementia literature lists; cross-referencing;Search terms “frontotemporal or FT(L)D” and “caregiver or carer”English and German articles, no limitations regarding the type of publication, two independent reviewers |
| Interventions | n/a |
| Outcomes | 19 papers dealing with burden, problems and needs of caregivers were identified; ten studies focused on burden, sixteen studies on problemsDelayed diagnosis, young age of onset, behavioral disturbances, caregiver depression, lack of information, lack of care facilities and reduced caregiver well-being as a result of neglect of own needs are named as problems;One study examined the needs of caregiversEight interventions are presented, the literature search did not reveal any RCTs, mainly education and support groups |
| Limitations | Lack of sufficient data for meta-analysis |

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## 4.10 O’Connor et al. (2014) – Functional disability in primary progressive aphasia.

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| Reference | O’Connor, Claire M.; Ahmed, Samrah; Mioshi, Eneida (2014): Functional disability in primary progressive aphasia. In: *Aphasiology* 28 (8-9), S. 1131–1149. DOI: 10.1080/02687038.2014.910588. |
| Type | Educational article |
| Location/country | Australia |
| Aim/subject | To outline functional disabilities in PPA and its sub-forms, to describe the relation between those disabilities and other symptoms in PPA, to examine their impact on caregiver burden and to describe strategies for improving caregiver burden. |
| Participants | n/a |
| Methods/measures | Review of existing literature and authors’ experiences in PPA research over the past 10 years |
| Interventions | None |
| Outcomes | svPPA, nfvPPA and lvPPA (which is suggested to be rather associated with AD than with FTD) are described as well as their functional impairments in AdL, description of the development and validation of the FTDFRS toolImpact on family caregivers: svPPA caregivers do not report burden levels as high as bvFTD caregivers, even though both diseases present with a similar set of symptoms; thus, other factors such as disease progression have a stronger impact on caregiver burdenTherapeutic recommendations: caregiver education about and throughout the process of the disease is found to be most effective by authors’ experience, caregivers should be enabled to adapt to constant changes as well as to accept behavioral disturbances; measures that can be taken are modification of the patient’s environment, communication strategies and assessment of new situations for the patient and changes that can be made to manage behaviorsSpecific recommendations are made for the management of meal preparation, eating, shopping, telephone, driving, medication application, finances and correspondence, leisure activities, dressing, hygiene, continence, e.g. using images supporting written instructions and products of the same brand to facilitate recognition for PPA patients  |
| Limitations | No information about literature search strategy |

## 4.11 Shinagawa et al. (2015) – Non-pharmacological management for patients with frontotemporal dementia. A systematic review.

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| Reference | Shinagawa, Shunichiro; Nakajima, Shinichiro; Plitman, Eric; Graff-Guerrero, Ariel; Mimura, Masaru; Nakayama, Kazuhiko; Miller, Bruce L. (2015): Non-pharmacological management for patients with frontotemporal dementia. A systematic review. In: *Journal of Alzheimer's disease: JAD* 45 (1), S. 283–293. DOI: 10.3233/JAD-142109. |
| Type | Systematic review |
| Location/country | Japan |
| Aim/subject | To review published literature about non-pharmacological treatment options in FTD and to provide future directions. |
| Participants | n/a |
| Methods/measures | Literature search of PubMed, Medline, EMBASE and cross-referencing; databases searched using dementia and (“frontal lobe” or frontotemporal or early-onset or young-onset) and (management or intervention or nonpharmacologic or environment or care)No limitations regarding time span; trials for behavioral symptoms selected 🡪 exclusion of management trials of other symptoms, e.g. language impairment; exclusion of ALS/MND management trialstwo authors screened articles independently  |
| Interventions | n/a |
| Outcomes | 9 articles: 4 clinical trials, 5 case reportsStrategies for behavioral management are discussed; environmental strategies, safety issues, hyperorality and swallowing, financial issues and driving issues are addressed Caregiver support: more evidence for caregiver-aimed interventions than for environmental strategies in FTDCaregiver distress: young age of onset, delayed diagnosis and/or misdiagnosis, the assumption that dementia only affects the elderly and lack of professional knowledge and appropriate services are named as distressing for caregivers; burden, depression and stress are higher than in ADInterventions for caregivers: multidisciplinary approach; support groups rated helpful, coping strategies and the ability to recognize one’s own limits are crucial to maintain mentally healthyCommunity health services and institutional care: lack of systematic studiesCommunity care service: difficult access of social security and care insurance benefits, lack of care services equipped for FTD patientsDifficulties: small number of FTD patients; misdiagnosed FTD cases; lack of appropriate assessment tools for intervention outcomes; controlling for confounders;  |
| Limitations | Paucity of well-designed studies |