

Study characteristics

Study	Country and Setting	Study Design	Sample Size	Sample Characteristics	HL Domains	Tools/Questionnaires	Findings	Quality Rating
Akinleye et al., 2011	USA University hospital	RCT (REVEAL)	n = 313	First degree relatives of AD patients Sex: 223 f, 90 m Age: 33–86 yrs (M=58.1) Ethnicity: 80% Caucasian, 20% African American	Understand Appraise	1) AD knowledge 2) Perceived concern about AD 3) Ratings of importance of reasons for and against seeking genetic testing 4) Becks Anxiety Inventory (BAI)	- Caucasians were more likely to have correct AD and genetic testing knowledge - Caucasians had more pronounced AD concern than African Americans	Good
Ashida et al., 2009	USA University hospital	RCT (REVEAL)	n = 271	First degree relatives of AD patients Sex: 191 f, 80 m Age: 33–86 yrs (M=58.2) Ethnicity: 81% Caucasian, 19% African American	Apply - health behavior	1) Communication of APOE genetic test results 2) Pros and cons of genetic testing for AD 3) Beliefs about causes of AD 4) AD treatment optimism 5) AD concern 6) Perceived personal risk of developing AD	- Most participants communicated their risk assessments with their close environment - Predictors for communicating the test results were: high treatment optimism, low perceived AD risk and genetic attribution for the development of AD	Good

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Ashida et al., 2010	USA University hospital	RCT (REVEAL)	n = 269	First degree relatives of AD patients Sex: 190 f, 79 m Age: 33–86 yrs (M=58.1) Ethnicity: 81% Caucasian, 19% African American	Appraise	1) Center for Epidemiology Studies-Depression Scale (CES-D) 2) Beck Anxiety Inventory (BAI) 3) Impact of Genetic Testing for AD (IGT-AD) 4) Perceived AD risk 5) AD concern 6) Beliefs about causes of AD 7) Communication of APOE results	- Predictors for higher perceived AD risk: female gender, Caucasian ethnicity, younger age. - Predictors for lower perceived AD risk: negative APOE4 test results, extended education sessions regarding AD, African American ethnicity, older age	Good
Axelmann et al., 2003	Sweden University hospital	Observational CS	n = 551	High risk group: AD-affected parent/sibling (n=106) Low risk group: spouses of AD-affected patients (n=37) Control group: Swedish population register (n=408) Sex: 286 f, 265 m Age: 30–80yrs (M=62.7) Ethnicity: N/A	Access Appraise Understand	1) AD questionnaire 2) Jalowiec Coping Scale (JSC), 3) Life Satisfaction Questionnaire-Short Form (LSQ-SF)	- Access to AD information mainly through spouses, friends, literature, patient organizations and mass media - 54% of individuals felt they received too little information about AD from health care personnel - 20% of individuals indicated that the received information was difficult to understand	Good

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Chao et al., 2008	USA University hospital	RCT (REVEAL)	n = 162	First degree relatives of AD patients Sex: 108 f, 54 m Age: 30–78 (M=52.8) Ethnicity: N/A	Apply - health behavior	1) Lifestyle change (diet, exercise, medication/vitamins)	- APOE4 positivity was associated with health behavior changes	Poor
Christensen et al., 2011	USA University hospital	RCT (REVEAL)	n = 273	First degree relatives of AD patients Sex: 191 f, 82 m Age: 33–86 yrs (M=57) Ethnicity: 81% Caucasian, 19% African American	Appraise	1) perceived pros and cons of genetic susceptibility testing for AD	- Pros of genetic testing were rated as being more important than the limitations and risks. - 1 year after performing genetic testing and risk disclosure, participants reduced their endorsements of the pros and increased their concerns about risk of discrimination one year later	Fair
Christensen et al., 2015	USA University hospital	RCT (REVEAL)	n = 795	First degree relatives of AD patients Sex: 526 f, 269 m Age: ≥ 60 yrs (46,5%) Ethnicity: 79 % Caucasian, 21% African American	Access Apply- decision-making Apply- health behavior	1) Beliefs about AD and genetic testing 2) Sources of referral for study 3) Lifestyle change 4) Insurance changes	- Self-referred study participants were more likely to undergo genetic testing than actively recruited participants - Genetic test-seeking behavior was associated with higher household incomes, being younger than 60 years, having Caucasian ethnicity - At baseline 47% of the participants intended to change	Fair

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							health behavior - After 1 year APOE4-positive participants showed more health behavior changes than APOE4-negative participant	
Delazer et al., 2006	Austria and Germany University hospital	Observational CS	n = 452	Cognitively normal (n=401) Cognitively impaired (n=51) Sex: 238 f, 214 m Age: 50–95 yrs (M=74.2) Ethnicity: N/A	Understand	1) Health Numeracy task	- Older age, lower cognitive function, lower education, female gender were significantly associated with lower health numeracy test results - Overall health numeracy was significantly lower within cognitively impaired participants	Good
Eckert et al., 2006	USA University hospital	RCT (REVEAL)	n = 104	First degree relatives of AD patients Sex: 73 f, 31 m Age: M=51.3 yrs Ethnicity: N/A	Understand	1) Perceived AD risk 2) Risk Recall	- APOE genotype was more memorable than the numeric risk estimate for AD - Genotype information was recalled in a binary form	Fair
Fanshawe et al., 2008	USA University hospital	RCT (REVEAL)	n = 162	First degree relatives of AD patients Sex: 107 f, 55 m Age: 30–78 yrs (M=53) Ethnicity: N/A	Apply - health behavior	1) Lifestyle change (diet, exercise, medication/ vitamins)	- 1 year after risk disclosure lifestyle change was associated with higher risk-estimates	Poor

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Han et al., 2015	USA University hospital	Prospective CS	n = 689	MCI and cognitive normal participants Sex: 529 f, 160 m Age: 60–101 yrs (M=81.8) Ethnicity: 93% Caucasian	Apply - decision-making	1) Decision-Making Competence Measure (DMC) 2) Neuropsychological test (CERAD plus)	- MCI was associated with poorer financial and healthcare decision-making capacity	Fair
Linnenbringer et al., 2010	USA University hospital	RCT (REVEAL)	n = 246	First degree relatives of AD patients Sex: 105 f, 53 m Age: 49 ≥ 60 yrs, 109 < 60 yrs Ethnicity: 82% Caucasian, 18% African American	Appraise	1) Perceived AD risk 2) Risk recall 3) AD-related attitudes 4) Beck Anxiety Inventory (BAI) 5) Center for Epidemiology Studies- Depression Scale (CES-D) 6) Health Numeracy measure	- Risk disclosure had an impact on the individual participants' perceived risk of developing AD - Perceived risk before risk disclosure session was significantly higher than the perceived risk after risk disclosure - Perceived risk after risk disclosure remained significantly higher than the communicated individual risk	Fair
Marcheco-Teruel & Fuentes-Smith, 2009	Cuba N/A	Qualitative	n = 52	Healthy first-degree relatives of patients with EOAD Sex: 35 f, 17 m Age: 20–79 yrs (M=48) Ethnicity: Cuban	Apply - decision-making	Interview about AD knowledge, attitudes towards genetic testing and possible reproductive behavior	- The majority of participants was interested in presymptomatic genetic testing - Most important reasons to proceed with genetic testing were: be prepared for the disease, marriage and family planning such	Poor

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							as curiosity	
Bronner et al., 2016	Germany University hospital	Qualitative	n = 24	Mild AD (n= 5), caregivers (n= 6), healthcare professionals (n= 13) Sex: 16 f, 8 m Age: M=65 yrs (SD = 8.8) Ethnicity: N/A	Apply, health behavior	Semi-structured interview about medical and social decision topics in the context of early detection of AD	- Patients gained access to health and social care through spouses - Patients felt restricted in autonomy by relatives' paternalism - Tendency to postpone decisional topics, which their physicians emphasized as important to be discussed at an early disease-state	Fair
Guan et al., 2017	USA University hospital	Qualitative	n = 79	MCI, caregivers Sex: 35 f, 44 m Age: M=71.7 yrs (SD=7.4) Ethnicity: 96% Caucasian, 4% African American	Understand	Audio-recorded AD risk disclosure sessions (Roter Interaction Analysis System; RIAS)	- Disclosure of complex genetic risk information reduced the patient-centeredness of disclosure sessions - Companions were more actively engaged in session communication when patients are at increased genetic risk for AD	Fair
Banningh et al., 2008	Netherland Participants' home or outpatient clinic	Qualitative	n = 8	MCI Sex: 7 f, 1 m Age: 58–83 yrs (M=74.8) Ethnicity: N/A	Appraise	Semi-structured interviews on experiencing and coping strategies of MCI patients	- MCI patients encountered numerous negative consequences (practical, social and psychological difficulties) - MCI patients applied different coping-strategies (emotion-,	Fair

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							problem- and avoidant-oriented)	
Wain et al., 2009	USA Participants' home	Quantitative & Qualitative	n = 25	Healthy sibling of patients with EOAD Sex: 15 f, 9 m Age: 37–83 yrs (M=56.8) Ethnicity: Caucasian	Appraise Understand Apply, decision-making Apply, health behavior	Structured questionnaire and semi-structured interview on AD experience and AD perceptions	- Siblings of EOAD-affected individuals may be involved in the care of their affected sibling, which might impact their personal life - They had good knowledge about AD and were well aware of the personal risk for developing AD - The awareness of the higher AD risk might impact the psychological wellbeing, lifestyle and major life decisions	Fair
Green et al., 2009	USA University hospital	RCT (REVEAL)	n = 162	First degree relatives of AD patients Sex: 117 f, 45 m Age: 30–78 yrs (M=53.0) Ethnicity: 94% Caucasian	Appraise	1) Becks Anxiety Inventory (BAI) 2) Center for Epidemiology Studies- Depression Scale (CES-D) 3) Impact of Event Scale (IES)	- Risk disclosure did not entail clinical relevant short-term psychological effects - Test-related distress was reduced among the Apoe4-negative participants	Fair

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Marteau et al., 2005	USA University hospital	RCT (REVEAL)	n = 149	First degree relatives of AD patients Sex: 109 f, 40 m Age: 30–78 yrs (M=52.3) Ethnicity: 93% Caucasian	Appraise	1) Perceived personal Risk of developing AD	- Receiving an APOE4-positive disclosure had no impact on personal risk perception beyond the lifetime risk estimate reported to the participants - Participants with an APOE4-negative disclosure had a lower perceived personal AD risk	Good
Okonkwo et al., 2007	USA University hospital	Cross-sectional	n = 147	MCI (n= 60), mild AD (n= 31), Controls (n= 56) Sex: 87 f, 60 m Age: M=69 yrs Ethnicity: 80% Caucasian, 20% African American	Apply, decision-making	1) Capacity to Consent to Treatment Instrument (CCTI): expressing choice, appreciation, reasoning, understanding	- MCI patients had significant impairments on clinical abilities associated with capacity to consent to treatment	Good
Okonkwo et al., 2008	USA University hospital	Longitudinal	n = 204	MCI Sex: 118 f, 86 m Age: M=69 yrs Ethnicity: 78% Caucasian, 22% African American	Apply, decision-making	1) Capacity to Consent to Treatment Instrument (CCTI): expressing choice, appreciation, reasoning, understanding	- Over a three-year period, MCI patients showed progressive impairment in the ability to understand consent information - MCI patients had impairments in decision-making capacities which mirrored functional impairment	Good

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Roberts, 2000	USA University hospital	Observational CS	n = 203	First degree relatives of AD patients Sex: 153 f, 50 m Age: 30–92 yrs (M=53,5) Ethnicity: 96% Caucasian, 2% African American, 2% Other	Understand Appraise Apply, decision-making	1) Interest in AD testing 2) Perceptions of pros and cons of predictive AD testing 3) Psychological and demographic predictors of predictive AD test intentions	- interest in presymptomatic genetic testing was high and multiple psychosocial and epidemiological factors influenced genetic test intentions - Potential negative effects of presymptomatic genetic testing were not evaluated comprehensively	Fair
Roberts et al., 2012	USA University hospital	RCT (REVEAL)	n = 280	First degree relatives of AD patients Sex: 199 f, 81 m Age: 33–86 yrs (M=58) Ethnicity: 80% Caucasian	Understand Appraise	1) Objective numeracy skills 2) AD knowledge 3) Perceived AD risk 4) Risk recall	- A newly developed condensed protocol for communicating genetic AD risk showed similar educational results as the traditional (extended) education protocol	Good
Roberts & Conell, 2000	USA University hospital	Prospective CS	n = 203	First degree relatives of AD patients Sex: 153 f, 50 m Age: 30–92 yrs (M=53.3) Ethnicity: 96 % Caucasian, 2% African American, 2% Other	Understand Appraise	1) AD knowledge 2) AD beliefs 3) AD treatment optimism 4) AD-related distress 5) Perceived AD threat	- Participants had an overall fair knowledge about AD, though some participants held misconceptions about AD and possible future treatment developments - Risk perceptions and AD concern were high. Predictors for perceived concern were ethnicity (with Caucasians being more	Fair

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							concerned than African Americans), female gender, younger age, lower household income and being married)	
Roberts et al., 2005	USA University hospital	RCT (REVEAL)	n = 162	First degree relatives of AD patients Sex: 117 f, 45 m Age: M=53.0 Ethnicity: 94% Caucasian	Access Appraise Apply, health behavior	1) Interest in AD testing 2) Risk Perceptions 3) Insurance Changes 4) Lifestyle changes 5) Psychological Impact of Risk Assessment	- Individuals, who were proactively seeking out the study participation were more likely to be female and have a college graduate education status - Interest in AD testing was to contribute to research and preparing and arranging for the possibility of an illness - Higher AD risk was associated with lifestyle and insurance changes one year after risk disclosure	Fair
Roberts et al., 2003	USA University hospital	RCT (REVEAL)	n = 206	First degree relatives of AD patients Sex: 149 f, 57 m Age: 30–78 yrs (M=52.8) Ethnicity: 93% Caucasian	Appraise	1) Interest in AD testing	- The most common reasons for study participation were: contribution to research, preparing and arranging for the possibility of an illness and hope for development of an effective treatment	Fair

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Vernarelli et al., 2010	USA University hospital	RCT (REVEAL)	n = 272	First degree relatives of AD patients Sex: 193 f, 79 m Age: M=58.1 (SD = 10.6) Ethnicity: 81% Caucasian, 19% African American	Apply, health behavior	1) Lifestyle changes	- Participants who tested positive for APOE4 showed lifestyle changes more often (especially dietary supplement use), despite the absence of evidence that supplements reduced AD risk	Fair
Zamarian et al., 2010	Austria University hospital	Prospective CS	n = 54	MCI, Mild AD, Controls (each n= 18) Sex: 28 f, 26 m Age: M=76.2 Ethnicity: N/A	Appraise Apply, decision-making	1) Framing task	- Framing effects were detected in all three groups, positively-framed medications were judged more favourably than negatively-framed medications - Framing effects were more pronounced in MCI patients and mild AD patients than in controls	Fair
Zick et al., 2005	USA University hospital	RCT (REVEAL)	n = 148	First degree relatives of AD patients Sex: 107 f, 41 m Age: M=52 Ethnicity: N/A	Apply, decision-making Apply, health behavior	1) Insurance changes	- 12 months after risk disclosure, Apoe4-positive participants were more likely to think about insurance changes and had made more long-term care insurance changes, than Apoe4-negative participants	Fair

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Roberts et al., 2004	USA University hospital	RCT (REVEAL)	n = 289	First degree relatives of AD patients Sex: 205 f, 84 m Age: 30–82 yrs (M=54.6) Ethnicity: 93% Caucasian	Access	1) Worry about AD	- Participants maintained interest in genetic susceptibility testing despite being informed about the absence of prevention options for AD and the relative uncertainty - Significant predictors of participation in the clinical trial were age < 60 yrs and college graduate education status	Fair
Gooding et al., 2006	USA University hospital	Qualitative (REVEAL)	n = 60	First degree relatives of AD patients Sex: 52 f, 8 m Age: 37–76 yrs (M=54) Ethnicity: 95% Caucasian	Appraise	Semi-structured interviews on genetic testing experience, beliefs about AD and reactions to receiving test results	- Some participants perceived genetic testing as valuable, in order to make informed future health care decisions - The degree of uncertainty about the individual brain health status might have been associated with the distress and worries	Fair
Lawrence et al., 2013	United Kingdom University hospital	Qualitative	n = 28	MCI (n=14), Caregivers (n=14) Sex: 8 f, 6 m (MCI) Age: 45-86 yrs (M=69) Ethnicity: N/A	Appraise	Group discussions on participating in clinical trials for prodromal AD and MCI	- Participants were motivated to enroll in a clinical trial for prodromal AD, because they wanted clarification about their brain status and expected a diagnosis - Concerns regarding risks of study drug were minimal, but certain tests and trial procedures provoked greater anxiety	Fair

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Lim et al., 2016	USA University hospital	Qualitative	n = 11	SCD Sex: 9 f, 2 m Age: 56-66 yrs (M= 63) Ethnicity: N/A	Appraise Apply, health behavior	Semi-structured interview to assess emotional reaction, interpretation, and consequences on AD-biomarker risk disclosure	- Risk disclosure of PET amyloid status did not significantly impact mood, subjective sense of memory impairment, or perceived risk of developing AD and was not significantly associated with psychological wellbeing - Participants with increased amyloid burden were more likely to make positive lifestyle changes (engaging more in exercise and changing diet)	Good
Lingler et al., 2016	USA University Hospital	Qualitative	n = 20	MCI, Caregivers (each n=10) Sex: 5 f, 5 m (MCI), 7 f, 3 m (Caregiver) Age: 69-92 yrs (M = 78,6, MCI), 43-77 yrs (M = 63, Caregiver) Ethnicity: 1 African American / 9 Caucasian (MCI), 1 African American/9 Caucasian (Caregiver)	Understand	Semi-structured interviews on comprehension and satisfaction after fictitious amyloid PET disclosure (simulated sessions)	- Standardized counselling and disclosure of PET amyloid imaging was generally perceived as satisfactory and comprehensive	Good

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Vanderschaeghe et al., 2017	Belgium University hospital	Qualitative	n = 38	MCI Sex: 16 f, 22 m Age: 55–83 yrs (M=71) Ethnicity: N/A	Appraise Apply, decision-making	Semi-structured interviews on MCI patients' perspectives toward disclosure of brain amyloid PET results	- Participants were highly interested in disclosure of their biomarker results, because this facilitated understanding of their own brain health status and making informed decisions about future life planning - Participants were conscious of possible emotional effects of amyloid result disclosure	Fair

Abbreviations: N/A= not available; RCT=randomized controlled trial; CS=controlled study; AD= Alzheimer's Disease; f=female; m=male; yrs= years; M= Mean; MCI= mild cognitive impairment; APOE= Apolipoprotein E; SCD= subjective cognitive decline; PET= positron emission tomography; BDI= Becks Depression Inventory; BAI= Becks Anxiety Inventory

Appendix 4: Study Characteristics