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Identifying Patterns of Communication in Patients Attending Memory Clinics: A Systematic Review of Observations and Signs with Potential Diagnostic Utility

Authors:
Corresponding Author:
Dr Cate Bailey, MBBS MRCPsych
SpR in Old Age and General Adult Psychiatry
East London Foundation Trust
City and Hackney Mental Health Care for Older People
Unit 1, 30 Felstead St
London
E9 5LG
cate.bailey@elft.nhs.uk

Dr Norman Poole, MBChB MRCPsych MSc MD
Consultant Neuropsychiatrist
South West London and St George's Mental Health NHS Trust
Neuropsychiatry Service
Clare House
St George's Hospital
Blackshaw Road
London
SW17 0QT
Norman.poole@swlstg-tr.nhs.uk

Dr Daniel Blackburn BSc, MBChB, MRCP, PhD
Senior Lecturer and Honorary Consultant Neurologist
Sheffield Institute for Translational Neuroscience (SITraN),
University of Sheffield
385A Glossop Road
Sheffield
S10 2HQ
d.blackburn@sheffield.ac.uk

Abstract

Background:
Subjective cognitive complaints are commonly encountered in primary care and often result in memory clinic referral. However, meta-analyses have shown such concerns do not consistently correspond to objective memory impairment or predict future dementia. Memory clinic referrals are increasing, with greater proportions of patients attending who do not have dementia. Studies of interaction during memory clinic assessments have identified conversational profiles which can differentiate between dementia and functional disorders of memory. Such profiles could reduce unnecessary investigations in patients without dementia.

Aims:
To date studies exploring communication patterns for the purpose of diagnosis have not been reviewed. This review therefore aimed to identify and collate signs and observable features of communication, which could clinically differentiate between dementia and functional disorders of memory.

Design and Setting:
This review systematically reviewed and synthesised evidence from studies with heterogeneous methodologies.

Methods:
A qualitative, narrative description and typical memory clinic assessment were employed as a framework.

Results:
16 studies were met criteria for selection. Two overarching themes emerged: 1) Observable clues to incapacity and cognitive impairment during routine assessment and interaction and 2) Strategies and accounts for loss of abilities in people with dementia.

Conclusion:
Whether the patient attends with a companion, how they participate, give autobiographical history, demonstrate working memory, and qualitative observations during routine cognitive testing are all useful in building a diagnostic picture. Future studies should explore these phenomena in larger populations, over longer periods, include dementia subtypes, and develop robust definitions of functional memory disorders to facilitate comparison.

249 words

Key words: Dementia diagnosis, memory clinic, subjective memory impairment, functional memory disorder

Background and Introduction

Subjective cognitive complaints are seen frequently in primary care and commonly

trigger referral to memory clinics (1). These complaints are of potential clinical import, might indicate cognitive decline and dementia, and are criterion for Mild Cognitive Impairment (MCI) (1). However, recent literature has cast doubt on their validity as a marker of MCI due to the poor correlation between subjective and objective memory performance and the fact that subjective reports do not consistently predict future dementia (2, 3).

The National Dementia Strategy (4) and Prime Minister's Challenge (5), reflected a drive to increase dementia diagnoses. Accordingly, UK memory clinics assessed, on average, 30.9% more patients in 2014 compared to 2013 (6). However, this increase appears to reflect a greater number of patients attending without neurodegenerative conditions (7).

Although much of the recent dementia diagnostic research focuses on increasing use of technology and biomarkers, some authors are exploring clinical skills (8). Creavin and colleagues are currently undertaking a Cochrane review of GP judgement in the diagnosis of dementia (8). A previous meta-analysis found that GPs were able to identify 75% of people with dementia based on clinical impression (9). Doctors are known to use various types of reasoning to reach diagnoses including pattern recognition, which can have heuristic value but is also prone to particular types of error (10). Objective assessment of diagnostic processes, and identification of factors contribute to "gut-feeling" may demonstrate significant utility in understanding and improving clinical judgement in both GPs and secondary care physicians.

Although depression and other psychiatric or medical disorders account for some non-dementia presentations to memory clinics, there remains a significant proportion of patients who lack a diagnosable condition (7) (11). Functional disorders of memory are attracting increased research interest, as have other such "Medically Unexplained Symptoms" (MUS) (1).

Schmidtke and Metternich proposed criteria for "Functional Memory Disorder" (FMD); a potentially reversible memory complaint thought to be secondary to psychological or emotional factors in the absence of major psychiatric disorder (12). Aetiological factors include overwork, interpersonal conflict, somatic illness, adjustment disorder, dysthymia and "Alzheimer Phobia" (13). A longitudinal study of 46 patients with a diagnosis of FMD followed up for a mean of 20 months found that symptoms persisted in 39 patients, though only one was later diagnosed with dementia (13).

It is increasingly understood that patients with MUS present frequently to both primary (14) and secondary care services (15) and often receive unnecessary investigations resulting in significant costs to the health system (15).

Although a recent review on "Functional Cognitive Disorder" (16) advised neuroimaging to exclude neurodegenerative causes, such investigations can intensify anxiety and cause iatrogenic harm (17, 18). Many patients report memory clinic assessments are lengthy, distressing and stigmatizing (19). Therefore, a rapid and inexpensive means of identifying such non-neurodegenerative conditions would benefit both patients and clinicians.

Conversation analysis in healthcare involves observation of clinical interaction occurring in real time (20). There now exists a robust body of evidence demonstrating that looking at how patients communicate, as well as what they say, can help to differentiate between epileptic and non-epileptic attacks during a single neurological assessment (21, 22).

Two recent studies identified divergent interactional profiles which could help differentiate between neurodegenerative and non-neurodegenerative disorders, ie: dementia and functional disorders of memory (23, 24). To date studies exploring the diagnostic utility of communication during cognitive assessments in discriminating between FMD and dementia have not been reviewed.

Methods

This systematic review sought to undertake a narrative, clinically-focused synthesis of existing evidence of features of communication, which could potentially discriminate between neurodegenerative and functional memory disorders. Narrative reviews are recognized as tools for drawing together evidence where the review question necessitates the inclusion of a variety of research designs; including qualitative and quantitative data (25).

The review questions were:

1. What is the current evidence for features of communication, interaction or clinically observable signs which can help differentiate dementia from functional memory disorders in a memory clinic assessment?
2. What are the features of communication in dementia which could represent future points of comparison to functional disorders of memory?

A computer assisted systematic literature search was undertaken to find published studies comparing observable signs and features of communication in functional memory disorder and dementia. Databases included: Books@Ovid, CINAHL, Embase, Medline, London Health Libraries, PsychInfo, PubMed, Google Scholar and the Cochrane Library. The initial search had a date range up to 2017. The terms for the functional memory disorder searches were developed through consensus with co-authors, and based on previous reviews (1, 16, 17, 26, 27). These terms were also informed by a recent survey which explored how UK doctors describe functional memory symptoms (28). Forward and back citation searching of any included articles was performed, as well as direct inquiry with specialists in the area.

Only a few papers directly comparing communication in these two diagnoses were found, so further searches were undertaken exploring communication in dementia in order to identify future areas for comparison.

Relevant papers from a previous review of healthcare interactions in dementia were selected (29). Papers considered applicable were those focusing on the assessment stage of memory clinic consultations. Furthermore, an updated search was conducted with the same search terms (limits 2014 – 2017) in order to identify any

relevant papers published since the initial review. The search terms are described in table 1.

Included studies observed communication in patients attending memory clinic or where cognition was assessed or discussed. Qualitative and easily observable aspects of behaviour during neuropsychological testing were included. Excluded studies were those focusing on population prevalence of subjective cognitive complaints, as these had been recently reviewed (30). Also excluded were studies comparing quantitative results and patterns of neuropsychological testing as this is not part of initial memory clinic assessment. Studies requiring computerized analysis, or those including interactions with interpreters were excluded. Communication in patients with formally diagnosed major mental illnesses were also excluded. Full details of the exclusion criteria are detailed in appendix 2.

Search results are included in a PRISMA diagram (figure 1).

The main author performed all searches and screened titles and abstracts against criteria. For any papers where there was ambiguity the full text was sourced. If the main author was unsure whether particular studies met criteria the full text of this paper was shared between the authors and a consensus agreement was reached.

A total of 17931 papers were identified, and all titles assessed. 1209 abstracts were then screened. 92 full text papers were identified for further assessment. 10 papers from the combined searches were identified, which were then added to 6 papers identified from the previous systematic review (29) to reach 16 final papers for review.

Quality was assessed by the lead author using the Quality Assessment Tool for Studies with Diverse Designs (QATSDD) (31). Data extraction, data analysis and interpretation was conducted based on the protocol for narrative synthesis (25) and completed by the lead author. The analysis employed techniques such as grouping, clustering, and thematic analysis (25). The synthesis was then developed through a process of “ideas webbing”, “reciprocal translation” and “conceptual triangulation” to generate themes which explained or interpreted findings across studies (25).

Results

The characteristics of the 16 included studies, including citation, sample and quality assessment score can be found in table 2. Characteristics of participants and further details of the studies are contained in table 3. Following the narrative synthesis processes described above three overarching themes emerged.

Narrative Synthesis - Themes

1. Clues to incapacity and cognitive impairment

Interactional features suggestive of cognitive impairment were further divided into subthemes.

Presence of an accompanying person (n=6)

Most memory clinics request that patients bring an accompanying person to their assessment (32-34). Nevertheless, a number of patients attend alone. Over cohorts of consecutive referrals, Larner and colleagues assessed Attending Alone (AA) as a diagnostic test of preserved cognitive function (32-34). The sensitivity of AA to identify cognitively normal individuals ranged from 0.93 – 1.0 (32-34) but specificity was low: 0.35 – 0.41 (32-34).

A small study primarily focused on interaction reported that 90.9% of patients with either early dementia or amnestic MCI (neurodegenerative disorders: ND) were accompanied, whilst 60% of patients with functional memory disorder (FMD) attended alone ($p<0.0008$) (24).

Another study observed that all patients who later received a dementia diagnosis were accompanied, compared with only 5/16 with FMD (23). Saunders noted that in patients attending a general outpatient neurology clinic 96.7% with cognitive impairment attended with family or a carer, whilst only 34.4% of cognitively normal persons did (35).

*Patient's Abil*ity to Answer and Participate in Consultation (n=3)

Two papers studied patients' ability to recall and describe memory concerns (23, 24). One compared patients with dementia to FMD (23). Another included patients defined as having ND (described above) (24). Both noted patients with dementia or ND had difficulty answering; sometimes giving no response or saying "um" or "er" (23, 24). Occasionally persons with ND would provide a generic answer, eg. "it happens all the time," or sought assistance from their companion (24). Patients with dementia were often unable to provide autobiographical information (23).

Patients with ND or dementia were unable to elaborate beyond the literal parameters of questions asked, took a long time to respond, and gave brief undetailed answers even when prompted (23, 24).

In a quantitative analysis of 11 patients with ND there were 45 responses indicating "I don't know" (29 verbal and 16 embodied in the form of head turning towards a companion). Conversely, patients with FMD provided quick, relevant, detailed and even sometimes unsolicited accounts of memory problems (23, 24). A significant difference was found between the number of verbal "I don't know" responses between the ND and FMD groups (24).

One study utilized the Lille Communication Test in 58 patients with dementia (36). They found verbal and non-verbal communication scores correlated with the Dementia Rating Scale ($P<0.001$) suggesting ability to participate in conversation may have a relationship to dementia severity (36).

Head Turning Sign (n=5)

A number of papers (23, 24, 37-39) assessed the Head Turning Sign (HTS) in which patients turn towards their caregivers in the face of difficulties or inability to answer a question during cognitive testing (37). Fukui and colleagues found the independent

contributors to head turning frequency were Alzheimer's related diseases (dementia or amnestic MCI), female gender and increasing dementia severity (37).

Larner observed HTS in response to requests for examples of memory "failures" during history taking (38). In later studies HTS proved specific (0.98, 95%CI: 0.95 - 1.0) but not sensitive (0.6, 95%CI: 0.49 – 0.7) for the presence of neurodegenerative disorder. Larner suggests HTS is an easily observed clinical sign which has a high positive predictive value for progressive cognitive impairment (39). Although not meeting criteria for a screening observation due to low sensitivity, presence of HTS does suggest further investigation is required (39).

In the two small conversation analysis studies, no statistically significant difference in HTS between cognitively impaired and normal individuals was found (23, 24). However other verbal and non-verbal requests for assistance were observed (23, 24). Responses from people with dementia were often delayed and lacking detail, which may leave their companion to step in (23).

Companion Involvement (n=6)

In profiling the triadic (three party) interaction in geriatric appointments, Hasselkus identified consultations with persons with cognitive impairment had a disproportionate number of prolonged dyadic (two party) interactions between companion and doctor (40). It was noted sometimes the physician shifts the conversation, sometimes the caregiver "interrupts"; answering a question initially directed at the patient (23, 40).

In a later paper Hasselkus noted patients with cognitive impairment often "allow" companions to explain their impairments (41). In cases of "marked impairment" evidence for incapacity came from the patient's own discourse: incoherence, non-responsiveness, or frequent need for the doctor to repeat questions (41). Sometimes companions would overtly communicate that the patient was not going to contribute, eg: "She (the patient) is not going to understand," or correct, add to, prompt or paraphrase the patient (41).

Conversely in consultations with patients without cognitive impairment patients demonstrated self-responsibility and autonomy with some control over the appointment agenda (41). However the results are limited by the fact that patients with cognitive impairment and sensory deficits are analysed collectively (41).

In outpatient neurology appointments companions contributed a greater number of comments in consultations where patients had cognitive impairment (35). Karnieli-Miller and colleagues graphically represented the shifts in a triadic memory clinic interaction over the course of an initial assessment (42). They too noted the companion tended to interject when the patient gave "incorrect" information or when the physician directed the conversation towards the companion (42).

Patients with FMD were less likely to attend with companions (23, 24, 35). When they did attend with companions they still answered questions on their own, and directly requested companion confirmation (23).

Anosognosia and who is more worried? (n=3)

Anosognosia refers to loss of insight or awareness of impairments which commonly occurs in dementia (43). When asked who was more worried about the memory impairment patients with FMD would express that they were the most concerned (24). In 4/5 consultations with patients with early dementia the patient would often not respond at all, and the companion expressed more concern (24).

Saunders also noted that patients with cognitive impairment frequently made attempts to normalize, minimize or account for their memory impairments, for example “(I’m) just like my grandma. I can’t remember anything, but who could?” (44).

Assessment of cognition during natural interaction (n=2)

One study looked at responses to compound questions, such as “Could you tell me a little about your background, where’re you’re from? And where did you go to school?” (24). Patients with ND or dementia responded to a single component of such questions, then required repetition or simplification of the question (24). Conversely those with FMD were able to address all parts of the question in a prolonged and detailed response (24).

Jones and colleagues noted the effort and compensation patients with FMD demonstrate in responding to compound questions. When asked a two-part question they were able to respond to both components in detail (23). Any repetitions were acknowledged with phrases, eg. “As I said earlier” which the authors argue demonstrates awareness of repetition, and preserved working memory (23).

Patients with dementia, however, can be repetitive and do not preface their repetitions with acknowledgements (23). Doctors are generally advised against the use of compound questions. However, the authors of the above studies argue selected use could reflect a method of assessing working memory within natural interaction reducing the later need for more formal and confrontational testing (23, 24).

2. Strategies and accounts for loss of abilities in persons with dementia

Face-saving and accounts (n=5)

“Saving face,” is a sociological construct often applied in analyzing how persons with dementia manage situations where they are unable to provide an appropriate response (45). Many papers focused on what is probably the most “face-threatening” component of a memory clinic assessment: formal cognitive testing. Studies examined compensatory strategies including humour (46), accounts and metaphor (35, 44) and the function and meaning of particular types of “I don’t know” (IDK) responses (47).

Saunders profiled humour during neuropsychological assessments, finding cognitively impaired patients initiated 3.7% of the total humour whilst clinicians

initiated only 1.4% (46). Patients with dementia tended to use more dominant and self-denigrating humour (46). An example of dominant humour is the patient's statement to the psychologist "You're out of your mind," when asked to copy a line drawing, where the author argues the implicit communication is the patient is unable to perform the task (46)

Saunders also describes how patients excuse their difficulties in the form of cognitive, experiential, comparative and emotional accounts and explanations of ability and attention (44). Patients with cognitive impairment used "object metaphors" such as images of tools or machinery (eg: "my brain is off key") as the cause of their inability to recall the answer (44). In accounting for the experience of memory loss patients would sometimes assign blame to lack of knowledge, for example when unable to name a paint palette the patient says "I don't know that because I worked with cars" (44). Patients with cognitive impairment would also use attention or ability when unable to complete tasks, eg: "I didn't pay that much attention" (44). Saunders argues that metaphors serve to maintain a "competent identity" and create distance from a "forgetful identity" (44).

Saunders and colleagues later found justifications for memory lapses were more likely to happen in consultations involving persons with cognitive impairment and most occurred during the testing stage of the examination (35).

Hesson and Pichler specifically explored the function if "I don't know" (IDK) responses during MMSE (Mini-Mental State Examination) administration (47). Responses which the authors describe as "Knowledge reinforcing tokens", such as "My brain is going to hell. I can't remember everything," appear very similar to Saunders' accounts and metaphors (44, 47).

Qualitative aspects of cognitive testing (n=1)

Closely related to face-saving and accounts are considerations of the qualitative aspects of cognitive testing. Many clinicians recognize the clinical value of qualitative observations during formal cognitive screening including the patient's approach and effort (48).

Hesson and Pichler examined all "I don't know" responses during cognitive testing to explore what this phrase communicates beyond a lack of knowledge (47). They interpreted that immediate IDK responses, or those following a pause signified lack of knowledge (47). "Face saving" IDK (described above) and "knowledge reinforcing tokens" were perceived to demonstrate inability to answer due to lack of knowledge. "Turn final" IDK tokens such as "Chicago, Cadillac, I dunno," (when asked to recall three objects), were also interpreted as a desire to terminate the sequence due to trouble remembering (47).

Non-lack of knowledge IDKs included hedging responses, such as "Oh *I don't know*, but I guess we're still in ___ city," and bridging responses, which were felt to buy time (47). Resistance responses were also included under the "Non-lack of knowledge IDK" responses as although the authors reported the surrounding talk as whole communicated inability to answer questions, the "*I don't know*" itself did not communicate this (47). From a practical point of view such a division may not demonstrate clinical utility although the authors found that severity of cognitive

impairment was statistically predictive of the use of “I don’t know” lack of knowledge phrases (47). However, the grading of cognitive impairment was based solely on clinician report rather than objective measures so the application of statistical measures may not be appropriate (47).

Taken as a cohort the papers exploring qualitative aspects of cognitive testing generate evidence that the talk occurring around formal testing, and the approaches, responses and accounts patients with dementia provide can be illuminating. However, this area of inquiry is limited by the lack of comparison to cognitively normal individuals.

Synthesis of evidence within clinical framework of memory assessment

As described, the final aspect of the synthesis draws together existing evidence in the order of a naturalistic memory clinic from start to finish. A summary of the features, levels of evidence and gaps in current knowledge are described in table 4.

Discussion

Summary

This review collated and synthesized evidence from 16 studies with heterogeneous methodologies using a narrative and clinical framework. The review found relatively firm conclusions in specific populations, and promising areas for future consideration. In relatively small and select samples there was robust and replicated evidence for the sensitivity of the HTS in identifying cognitive impairment, and for the attended alone sign (AA) in identifying cognitive “normality”. Other less replicated and more difficult to operationalize signs of interaction and communication could, collectively, provide the foundations of conversational profiles to differentiate between dementia and functional disorders of memory.

Strengths and Limitations

A strength of this review is the comprehensive search strategy and ability to draw together findings in a clinically relevant framework. Limitations include the use of a single author to extract and assess the quality of data. The author attempted to minimize the risk of study selection and extraction bias by discussion with co-authors.

Both patients with neurodegenerative conditions and functional memory disorders are heterogeneous groups. Patients with functional memory disorders remain poorly understood. Additionally, the heterogeneity of terms clinicians use to describe similar but not necessarily interchangeable concepts is also problematic in drawing comparisons (28).

In addition, the heterogeneity of use of formal cognitive assessments or rating scales and variations in how diagnoses were reached mean results must be analysed with

caution. The vagueness in reporting “cognitive impairment” casts potential doubt on the rigor of clinical diagnosis.

The cross sectional nature of the studies included, and lack of biomarkers or novel neuroimaging is also a limitation. Cross sectional methodologies cannot provide iron-clad evidence that cognitively normal individuals who are presenting to memory clinic now will not develop dementia in the future. It should also be noted that the participants in the study were attending secondary care services and may not be directly representative of all patients seen in general practice with memory concerns.

Comparison with Existing Literature:

The concept of cognitive examination as a quantitative and qualitative exercise has been reported during focus groups with clinicians working in memory clinics (48). This review adds weight to these reports and highlight that observations of the patient’s approach, comments and interaction during cognitive testing are valuable in diagnosis. The use of humour, “face saving” explanations and accounts for incorrect answers, and even the meaning of “I don’t know” responses can be informative. Historically “I don’t know” responses have been suggested as a sign of depressive pseudo-dementia (49). However, this review highlights that such responses reflect nuanced and subtle communications, and further studies could be illuminating.

The use of conversation analytic (CA) interventions is well established in first seizure clinics (20, 50) and can be taught relatively easily. A one-day training course resulted in junior neurologists allowing more time before first interrupting patients during assessments and increased ability to differentiate between epileptic and non-epileptic events (51). A CA informed approach to cognitive assessments could facilitate both diagnostic clarity and formulation for patients presenting to memory clinics who do not have dementia (see teaching website link below on how to look for interaction in memory clinic). Such methods would be aligned with the now favoured method where MUS are approached as positive diagnosis rather than one of exclusion (52).

Implications for research and practice

In routine memory clinic consultations whether the patient attends with a companion, how they interact, account for difficulties, give basic autobiographical details, demonstrate working memory, and approach formal cognitive testing, are useful in building a diagnostic picture. No one sign is likely to prove diagnostic, nor would observation replace clinical examination or blood and imaging investigations where appropriate. However, equipping clinicians with an increased repertoire of observational tools could aid both those working in and referring to memory clinics. If qualitative aspects of routine assessments can be interpreted alongside brief screening tools such as the GPCOG (53), GPs may be more able to confidently decide who is appropriate to refer for further assessment. For example high functioning individuals may pass conventional brief cognitive screening but the use of CA or interaction analysis as shown here may help validate a gut feeling that’s

something is wrong and refer on for further testing. Observing responses to occasional multi-part questions, and the interaction between patient and relative could represent less confrontational ways for GPs to assess cognition in patients who might refuse to participate in formal cognitive testing. Conversely, identifying signs suggestive of functional disorders of memory might prompt GPs to explore the meaning of the cognitive concerns and provide reassurance or consider watchful waiting. This would be in keeping with recognized approaches to MUS. With the increased numbers of patients without dementia attending both primary and secondary care, it is vital that clinicians develop evidence-based skills which empower them to avoid unnecessary neuropsychological testing and imaging investigations.

Future studies should explore these observations in larger populations and in primary care settings; for example, replicating HTS and AA in older groups and dementia subtypes. Direct comparison of qualitative and quantitative findings of cognitive testing will be helpful. Additionally, developing robust definitions of subjective memory complaints and functional memory disorders will allow more definite comparison between and within groups. The use of follow up studies, biomarkers and novel neuroimaging techniques represent opportunities for clinical signs to be compared with quantitative measures to add weight to existing observations.

How this fits in

This review found observations during interaction in cognitive assessments can help differentiate between dementia and functional disorders of memory. Whether the patient attends with a companion, how they participate, give autobiographical history, and qualitative observations during cognitive testing are useful in building a diagnostic picture. For GPs the observations in this review may augment existing screening tools and maximize limited time available to inform decisions about onward referral.

Summary Box: What a busy clinician can look out for in patients presenting with cognitive problems

Signs suggestive of functional disorder of memory	Signs suggestive of neurodegenerative disorder
• More likely to attend clinic alone • Worried about their memory • Providing clear personal history and explicit, detailed examples of memory failures • Demonstrates working memory within the interaction (refer to things they have said earlier) • Able to answer multi-part questions	• Attending with companion, and companion is more worried about memory than patient • May turn head towards companion when unable to answer • Unable to provide personal history, from recent past such as detailed information about what they did last weekend or from the

	news • Provides examples of memory failures as 'all of the time' or everyday but cannot provide specific examples. • Evidence of short term memory problems within consultation (repetition) • Struggles with multi-part questions • May use humour or try to "save face" during cognitive testing

Link to education module of following website that provides examples of real life cases showing the signs described in this paper (http://sitran.blymi.com)

3998 words

Functional Memory Disorders (Non-neurodegenerative) Search (up to and including 2017):	**Dementia Search (2014 – 2017): Search terms from existing review of healthcare interactions in dementia (29)**
Terms (Combined by OR): Subjective cognitive decline Subjective cognitive complaints Subjective memory complaints Subjective forgetfulness Functional memory disorder Functional memory symptoms Functional cognitive disorder Cogniform disorder Cogniform condition Fear of dementia Dementia worry Worried well AND: Assess* Diagnos* Interact* Communica* Talk* Discour* Interview* Dialog* Conversation	Terms (Combined by OR): Alzheimer* Dement* Cognitive impair* Memory Neurocogni* Neuro-cogni* Cogni* disor* Cogni* func* AND: Assess* Diagnos* Interact* Communica* Talk* Discour* Interview* Dialog* Conversation

Table 1 – Search Terms

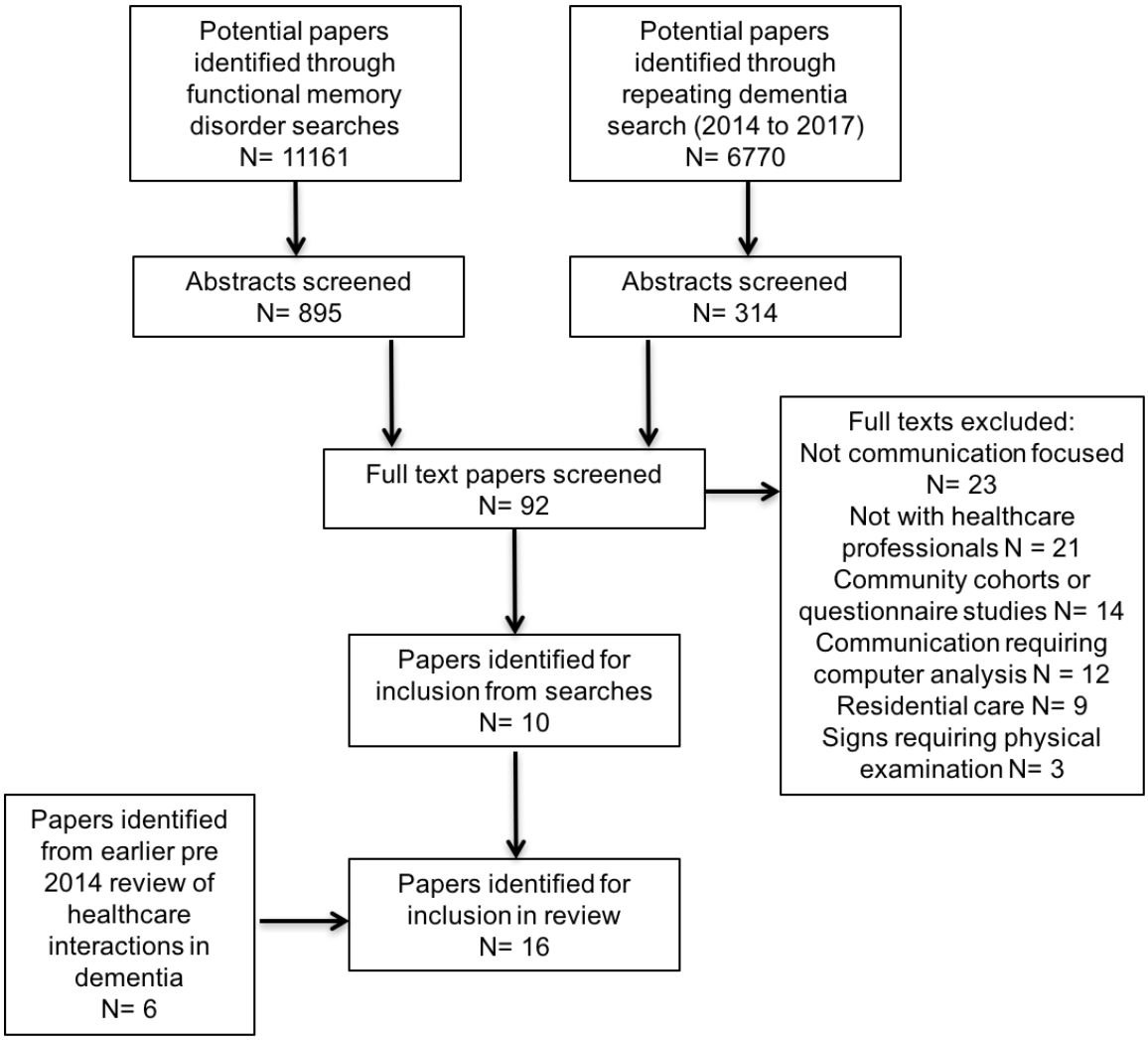

Figure 1 - PRISMA Flow Diagram of Search Lines

Table 2 - Summary of studies and quality assessment scores

Study	Measurements	Type of Study	Gold Standard or Diagnostic Comparison	Focus and Analysis	QA Score (%)
Elsey et al, 2015	Video and audio	Observation, naturalistic, cohort	Clinical consensus: MDT discussion based on neurologist assessment, history, ACE III, MRI	Conversation analysis of communication to develop profiles to differentiate dementia and FMD. Verbal "I don't know" responses and head turning subject to Fisher's Exact Test. Attending Alone (AA) subject to Chi-Squared Test.	Mixed methods: 79.2
Fukui et al, 2011	Observation	Observation, naturalistic, cohort of consecutive outpatients	Diagnosis based on established diagnostic criteria: AD: NINCDS-ADRDA criteria aMCI: Petersen's criteria DLB: DLB Consortium criteria in 2005, VaD: NINDS-AIREN	Head Turning Sign (HTS) during cognitive testing with Hasegawa Dementia Rating Scale, with caregiver seated 1m behind patient. HTS positive if patient turned back to caregivers and asked for help implicitly or explicitly. HTS also scored in terms of severity. Comparison between subtypes of dementia.	Quantitative: 71.4
Ghadri-Sani and Larner, 2013	Observation	Observation, naturalistic, cohort of consecutive outpatients	Cognitive impairment (either dementia or mild cognitive impairment (MCI)) was defined according to clinical diagnostic criteria (respectively DSM-IV-TR and modified Petersen).	Head Turning Sign (HTS) during history taking as a sign of cognitive impairment. HTS judged to be present if patient turned his/her head away from interlocutor and towards accompanying person when first invited to describe symptoms (eg: "Tell me about the problems you're having with your memory." HTS later in consultation (ie: during cognitive testing) was not considered.	Quantitative: 57.4
Hasselkus, 1992	Audio	Observational, naturalistic, selection of patients likely to be attending with companions	Diagnostic process not described	Qualitative analysis of geriatric outpatient patient, doctor and caregiver interactions, quantitative analysis according to level of impairment	Mixed methods: 66.7
Hasselkus, 1994	Audio	Observational, naturalistic, selection of patients likely to be attending with companions	Diagnostic process not described.	Discourse analysis for self care behaviours as a marker of adult status in the older patient in geriatric outpatients. Data then categorised into degree of impairment.	Qualitative: 61.9
Hesson and Pichler, 2016	Audio	Verilogue corpus, cohort of patients undergoing testing with MMSE	Clinician rating of mild, moderate or severe impairment. Individual MMSE scores not reported.	Conversation analysis with specific focus on "I don't know" or other variations in speech during MMSE administration, analysis of surrounding talk, context and meaning in mild, moderate and severe cognitive impairment.	Mixed methods: 66.7
Jones et al, 2016	Video and audio	Observational, naturalistic, cohort study	Gold standard diagnosis made by consultant neurologist, based on assessment, ACE R, detailed neuropsychological battery and MRI.	Conversation analysis with focus on history taking part of assessment to identify interactional features which discriminate between Neurodegenerative disorders and and Non-Neurodegenerative Disorders.	Qualitative: 81.0
Karnieli-Miller et al, 2012	Video and audio	Observational, naturalistic, cohort study	Diagnostic process not described.	Discourse analysis focusing on triadic and dyadic exchanges during the process of memory assessment and diagnosis delivery.	Mixed methods: 72.9
Larner, 2005	Observation	Observational, naturalistic, cohort/audit study	Dementia diagnosed based on DSM IV criteria, established by clinical interview, neuropsychological assessment and neuroimaging. Subtype of dementia was also established. Patients had minimum follow up of 6 months.	All patients referred are sent a letter asking them to bring a relative, friend or carer from whom additional information may be obtained. Confidence intervals and Wilson methods of specificity and sensitivity used to calculate attending alone as a 'diagnostic test' for dementia.	Quantitative: 54.8
Larner, 2009	Observation	Observational, audit of consecutive referrals	Dementia was diagnosed by DSM-IV-TR criteria based on clinical interview, informant interview where possible, neuropsychological testing and structural brain imaging (CT ± MRI), as in previous cohorts reported from this clinic.	The Attending Alone (AA) sign was considered as a test for dementia. The STARD checklist for reporting diagnostic accuracy studies was observed and basic principles of evidence- based diagnosis were applied to calculate test sensitivity, specificity, positive and negative predictive values (PPV, NPV), diagnostic odds ratio (DOR) and positive and negative likelihood ratios (LR+, LR−) with 95% confidence intervals (CI). Comparison made with previous cohorts from same clinic.	Quantitative: 71.4
Larner, 2012	Observation	Observational, audit of consecutive referrals	The presence of cognitive impairment (either dementia or mild cognitive impairment (MCI)) was defined according to clinical diagnostic criteria (respectively DSM-IV-TR and modified Petersen).	Head Turning Sign (HTS) during history taking as a sign of cognitive impairment. HTS judged to be present if patient turned his/her head away from interlocutor and towards accompanying person when first invited to describe symptoms (eg: "Tell me about the problems you're having with your memory." HTS later in consultation (ie: during cognitive testing) was not considered.	Quantitative: 66.7
Larner, 2014	Observation	Observational, audit of consecutive referrals	Assessment by semistructured clinical interview, cognitive screening instruments, and structural neuroimaging, supplemented as necessary by additional investigations (eg, formal neuro-psychological assessment, EEG, and neurogenetic testing). Standard diagnostic criteria for dementia (DSM-IV), dementia subtypes, and MCI were used.	Analysis of Attending Alone (AA) sign used standard principles of evidence-based diagnosis and observed the STARD checklist for reporting diagnostic accuracy studies.	Quantitative: 73.8
Rosseaux et al, 2010	Video and audio	Case-control study, observational	All patients were assessed with a comprehensive clinical examination by senior staff neurologist, psychiatrist, neuropsychologist, speech therapist, and nurse and imaging with CT or MRI. A consensual diagnosis was given for each patient according to existing diagnostic criteria.	Lille Communication Test (LCT) comparison of controls and subtypes of dementia. LCT addresses three domains: participation in communication, verbal communication and non-verbal communication.	Quantitative: 73.8
Saunders, 1998a	Audio	Observational, naturalistic, cohort	Memory clinic consists of MDT including geriatrician, psychologist, neurologist and neuropsychologist. Actual diagnostic process not described but history taking and neuropsychological testing formed part of assessment.	Neuropsychological assessment, qualitative, quantitative and discourse analysis with particular focus on humour exchanges.	Mixed: 77.1
Saunders, 1998b	Audio	Observational, naturalistic, cohort	Memory clinic consists of MDT including geriatrician, psychologist, neurologist and neuropsychologist. Actual diagnostic process not described but history taking and neuropsychological testing formed part of assessment.	Neuropsychological assessment, qualitative, quantitative and sociolinguistic analysis with focus on accounts and ways people with dementia justify or explain their memory problems.	Mixed 90.5
Saunders et al, 2011	Audio	Observational, naturalistic, cohort	Patients with cognitive impairment were those diagnosed by the neurologist or referring doctor with possible Alzheimer's disease, probable Alzheimer's disease, or mild cognitive impairment.	Neuropsychological assessment with qualitative and quantitative analysis of health, memory accounts and humour and comparison of these in CI and non-CI groups.	Mixed: 78.6

Table 3 - Study Setting and Participants

Study and Country of Origin	Total Number of Patients	Sampling	Diagnoses	Average or Range of Cognitive Testing Scores	Age	Gender	Companions present or considered in analysis	Ethnicity	Setting
Elsey et al, 2015 (UK)	30	Consecutive referrals to memory clinic October 2012 – October 2014 agreeing to participate in video recording. 30/99 videos analysed. Refusal data not provided.	Neurodegenerative (ND). Functional Memory Disorder (FMD)	Not described.	ND: Median 60 (47-80), FMD: 66 (51-78)	ND: 45.5% F FMD: 66.7% F	Yes	Not described	Neurology led memory clinic
Fukui et al, 2011 (Japan)	181	Consecutive referrals attending clinic run by lead author during the period September 2010 – March 2011. Refusals data not provided.	Alzheimer's dementia (AD), Amnestic Mild Cognitive Impairment (aMCI), Dementia with Lewy Bodies (DLB), Progressive Supranuclear Palsy (PSP), Vascular Dementia (VaD)	HDSR (Hasegawa Dementia Rating Scale) – Short cognitive test AD: 14.5 (+/- 6.6) aMCI: 24.8 (+/- 3.9) DLB: 15.1 (+/- 6.9) PSP: 14.5 (+/- 8.0) VaD: 20.5 (+/- 4.2)	AD: 79.1 (+/- 8.7 years), aMCI: 79.3 (+/- 4 years), DLB: 77.9 (+/- 6.3 years), PSP: 78.4 (+/- 5.2 years), VaD: 73.8 (+/- 3.2 years)	AD: 65%F, aMCI: 63%F, DLB: 47%F, PSP: 38%F, VaD: 33%F	Yes	Not described	Neurology department
Ghadri-Sani and Larner, 2013 (UK)	191	Over a 10-month period (February – December 2012), 191 consecutive new referrals were observed for the presence of HTS	Dementia, Mild Cognitive Impairment (MCI), Cognitively normal	85/191 judged to have cognitive impairment. Cognitive scores not provided.	Median: 60 (20-89)	45%F	Yes	Not described	Neurology led memory clinic
Hasselkus, 1992 (USA)	27	Purposive sampling approach to patients on clinic roster likely to be accompanied by a family member. Number approached and refusals not described.	"Continuing health problems", "dementing illnesses", hearing impairment and expressive dysphasia	Although participants are described as "cognitively impaired" or "not cognitively impaired" the cutoff point for cognitive impairment not described.	Mean 77.3 (64-91)	Not described	Yes	100% Caucasian	General internal medicine clinic
Hasselkus, 1994 (USA)	27	Purposive sampling approach to patients on clinic roster likely to be accompanied by a family member. Number approached and refusals not described.	"Continuing health problems", "dementing illnesses", hearing impairment and expressive dysphasia	Although participants are described as "cognitively impaired" or "not cognitively impaired" the cutoff point for cognitive impairment not described.	Mean 77.3 (64-91)	Not described	Yes	100% Caucasian	General internal medicine clinic
Hesson and Pichler, 2016 (UK and USA)	72	Outpatient consultations from the Verilogue corpus where physicians identified "dementia" as one of the primary conditions being assessed during the visit.	Mild Cognitive Impairment, Moderate Cognitive Impairment, Severe Cognitive Impairment	Although MMSE performed during consultation scores were not extracted. Severity was assessed by the consultaing physician as follows. Mild Cognitive Impairment: 18 (25%) Moderate Cognitive Impairment: 39 (54.2%) Severe Cognitive Impairment: 15 (20.8%)	55-74 years: 20 (27.8%), 75+ years: (72.2%)	65.3%F	No	Not described	Ambulatory care clinics with neurologists or primary care physicians
Jones et al, 2016 (UK)	25	Consecutive referrals to memory clinic October 2012 – October 2014 agreeing to participate in video recording. 25 videos recorded. Refusals not described.	Neurodegenerative (ND). Functional Memory Disorder (FMD)	Neurodegenerative: average ACE R score: 56/100 (range: 28-80). Non-neurodegenerative (FMD): average ACE R: 93/100 (range: 85-99)	ND: Median 61, FMD: 60, Overall range: 47-77	64%F	No	Not described	Neurology led memory clinic
Karnieli-Miller et al, 2012 (Israel)	25	Described as "convenience sampling": 25 first time assessments at diagnostic memory clinic recruited for participation. Refusals not described.	Not described, but dementia diagnosis delivered in at least some participants.	MMSE range 12-27	All >65	68%F	Yes	Not described	Outpatient memory clinics: mix of psychiatry, geriatrician and neurology led
Larner, 2005 (UK)	183	All consecutive referrals over 2 year period (September 2002 – August 2004)	Dementia, MCI, Not Dementia	Range of cognitive scores not described.	Not described	Not described	Yes	Not described	Neurology led memory clinic
Larner, 2009 (UK)	Sep 2004 - Aug 2008: 552, Sep 2002 - Aug 2004: 183	All consecutive patients seen by one neurologist over 4 year period. (September 2004 – August 2008)	Dementia, Not Dementia	Range of cognitive scores not described.	Sept 2004 – Aug 2008: Mean 61.4 (range: 20-90), Sep 2002 – Aug 2004): Mean 59.2 (range: 25-82)	Sept 2004 - Aug 2008: 49%F, Sept 2002 - Aug 2004: 43%F	Yes	Not described	Neurology led memory clinic
Larner, 2012 (UK)	207	Over a 10-month period (January - October 2011), consecutive new referrals were observed for the presence of HTS	AD and mixed AD/cerebrovascular disease, amnestic MCI, frontotemporal lobar degenerations, dementia with Lewy bodies, subcortical ischaemic vascular dementia and miscellaneous others. Depression and depression with cognitive impairment.	82/207 (39%) judged to have cognitive impairment. Cognitive scores not described.	Median: 60 (18-91)	53%F	Yes	Not described	Neurology led memory clinic
Larner, 2014 (UK)	726 (years 2008 - 2011), 735 (years 2002 - 2008)	Consecutive new patient referrals to a cognitive clinic seen over a 3-year period (September 2008 to August 2011)	Dementia, MCI, "Cognitively Healthy"	Range of cognitive scores not described.	Median: 61 (16-92)	47.2F	Yes	Not described	Neurology led memory clinic
Rosseaux et al, 2010 (France)	105	Cases recruited from memory clinic: suffering from mild-moderately severe dementia using standard criteria for respective disease. Controls: recruited from community matched to patients in gender, age and educational level. Refusals not described.	Alzheimer's dementia (AD), Fronto-Temporal Dementia (FTD), Dementia with Lewy Bodies (DLB), Controls (C)	MMSE: AD: MMSE: 22 (14-28) FTD: MMSE: 27 (14-30) DLB: MMSE: 24 (13-28) C: MMSE: 29 (25-30)	AD: 74 (50-79), FTD: 61 (51-78), DLB: 71 (57-78), C: 68 (50-79)	AD: 65%F, FTD: 52%F, DLB: 36%F, C: 47%F	No	Not described	Memory Clinic
Saunders, 1998a (USA)	17	Patients recruited from MDT memory clinic. Approach to sampling and refusals not described.	Alzheimer's disease: 7, Vascular dementia: 2, Alcohol related dementia: 1, Non-impaired: 1, Mixed dementia: 1, Other cognitive impairment (folate deficiency, endocrine): 4, Undetermined dementia aetiology: 1	Range of cognitive scores not described.	54-86	70%F	Yes	Not described	MDT Memory and Alzheimer's Clinic
Saunders, 1998b (USA)	17	Patients recruited from MDT memory clinic. Approach to sampling and refusals not described.	Alzheimer's disease: 7, Vascular dementia: 2, Alcohol related dementia: 1, Non-impaired: 1, Mixed dementia: 1, Other cognitive impairment (folate deficiency, endocrine): 4, Undetermined dementia aetiology: 1	Range of cognitive scores not described.	54-86	70%F	Yes	Not described	MDT Memory and Alzheimer's Clinic
Saunders et al, 2011 (USA)	60	Patients recruited through referral from neurology clinic and then later divided into cases or controls depending on presence of cognitive impairment. Sampling strategy and refusals not described.	Cognitively Impaired (CI): 31, Not Cognitively Impaired: 29	MMSE: CI group: 5 to 28 (mean: 18; SD: 6.6). Not routinely administered to non CI group.	Mean: 73.1 (range: 63–92 years)	CI group: 58%F, Non-CI: 48%F	Yes	CI: White 24, Black 6, Asian 0, Cuban-American 1, Non CI: white: 22, Black 6, Asian 1, Cuban-American 0	Outpatient neurology clinic (tertiary referral centre)

Table 4 - Summary of observable features over the course of a memory clinic assessment.

Observations During Assessment	Functional Disorders of Memory	Dementia or Neurodegenerative Condition	Level of evidence
Attendance at the memory clinic	More likely to attend alone (AA sign). (AA sign sensitive but not specific for "cognitive normality")	Likely to attend with companion	Robust and repeated studies in single neurology-led memory clinic, more evidence needed in other sites and for older adults.
Ability to answer questions about memory impairment	Unproblematic, detailed responses of "memory failures".	May not be able to answer, or if does answer likely to give generic/stock phrase responses such as "it happens all the time".	Two small studies, replication needed in larger population.
Ability to answer questions about biographical information	Detailed responses, sometimes more information than is required, even if closed questions are asked.	May not be able to recall personal information, or will give account for why unable to "can't recall offhand."	Two small studies, replication needed in larger population.
Ability to answer compound/multi-part questions	Able to address all parts of multi-part question, with generous detail.	Unable to respond to multi-part question. Likely to require prompting to answer second or third parts.	Two small studies, replication needed in larger population.
Time taken to answer questions	Answers quickly and unproblematically.	Responses may take so long that companion may step in to answer question.	Two small studies, replication needed in larger population.
Working memory in interaction	Aware of repetition and will preface these with "As I said earlier."	Unaware of reptition or "second time tellings" or other's responses to them. Will not preface reptition with acknowledgement of this.	Two small studies, replication needed in larger population.
Head turn during history taking	No evidence of head turning to companion.	May turn head to companion or recruit assistance from companion in other way (see below). (HTS sensitive but not specific for cognitive impairment).	Robust and repeated studies in single neurology-led memory clinic, more evidence needed in other sites and for older adults
Interaction with companion (if present)	Likely to directly request companion (if present) to confirm what they have already said.	May not be able to answer and companion will step in. Or may directly request companion assistance verbally. May give incorrect, or very limited information which companion will add to or correct.	Two small studies, and discourse and conversation analysis studies in geriatric outpatient clinics. Replication needed in larger population with robust measures of cognitive impairment compared to behaviour.
Companion turns at talk and participation in assessment	No direct comparison studies, but likely to be minimal companion contributions.	Companion likely to talk more if person has cognitive impairment.	Lack of comparison studies with those who have functional memory disorders, or studies of persons with dementia in memory clinic assessments. Further studies needed.
Who is more worried about the cognitive impairment?	Patient more worried about cognitive problems.	Companion more worried about cognitive problems. Patient may not be aware of any issues.	Limited directly observed evidence for particular behaviour in FMD but longstanding, robust evidence of anosognosia seen in dementia.
Humour, accounts and face-saving during history taking	Not studied specifically in formally diagnosed FMD, but cognitively normal individuals do not provide many accounts of cognitive difficulties.	Some very limited evidence, but more analysis needed.	More studies needed. May be a useful area of further enquiry.
Head turn during cognitive testing	Not studied.	More likely to turn head in Alzheimer's disease, and with more severe dementia.	One study with no comparison with persons without cognitive impairment, or with FMD. Direct comparisons needed.
Humour, accounts and face-saving during formal cognitive testing	Not studied.	Likely to provide various accounts and use "face-saving" strategies including humour when confronted with difficulties in cognitive testing.	Multiple studies of varying quality. Further robust studies comparing degree of cognitive impairment and performance on unbiased measures with qualitative observation of behaviour.
"I don't know" responses during cognitive testing	Not studied.	"I don't know" responses signifying lack of knowledge likely to be more common as cognitive impairment is more severe.	One study, with limitations the practical applications of findings. Further more clinically applicable studies would be helpful.

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Exclusion Criteria

- Studies focusing on community or population prevalence or longitudinal outcomes of subjective cognitive complaints will be excluded as these have already been reviewed (30).
- Studies comparing neuropsychological patterns and co-morbidities in patients presenting with subjective and objective cognitive impairment in a memory clinic population will also be excluded as these are the subject of a recent meta-analysis (2).
- Studies which report solely on the results of specialist neuropsychological testing.
- Studies not published in English.
- Studies examining the cognitive assessment where interpreters are used.
- Studies which require computerized analysis of speech to differentiate between diagnoses.
- Studies examining the assessment of persons with formally diagnosed major mental illness such as depression, psychosis or drug and alcohol related disorders. This population are excluded as those meeting the criteria for major disorders should be diagnosable based on clinical history, mental state examination and existing diagnostic criteria.