ABSTRACT
Fragile X premutation tremor-ataxia syndrome (FXTAS) is an inherited neurodegenerative disorder primarily affecting ageing men. Clinical presentation is widely variable with features common in the elderly including parkinsonism, dementia, psychiatric symptoms and behavioural change. FXTAS is caused by a CGG repeat expansion in the Fragile X mental retardation 1 gene. Subjects are carriers for Fragile X Syndrome. Most cases are identified after a grandchild is diagnosed with Fragile X Syndrome. The premutation is relatively common in the general population. FXTAS is potentially under-recognized and misdiagnosed.

Case Description - We discuss a case of FXTAS in a 70 year old man presenting with personality change, aggression, poor planning, self neglect, social disinhibition and cognitive deterioration. He was ataxic which had been diagnosed as cerebellar syndrome of unknown cause with signs of possible normal pressure hydrocephalus (NPH) on MRI. Mr F has been managed by Old Age Psychiatry with input from neurology. Diagnosis was eventually confirmed as FXTAS. His case has highlighted a number of clinical challenges. Notably, the medical and social management of neuropsychiatric symptoms and bizarre behaviours impacting on global function in older frail patients with FXTAS. Mr F was setting fire to furniture, defecating on the floor, serving cat food to his wife and driving with flat tyres. This required a collaborative multidisciplinary approach from psychiatry, primary and social care with psycheducation and support for family and carers.

Discussion - This case illustrates a potentially under-recognised condition causing neurological and neuropsychiatric symptoms. Accurate diagnosis is important to develop a better understanding of how to manage this cohort of patients. More research is required to improve mental health awareness, develop treatment guidelines and resources for family education.

WHAT IS FRAGILE X PREMUTATION TREMOR / ATAXIA SYNDROME?
FXTAS is a neurodegenerative disorder with a constellation of symptoms and neuropsychiatric signs that can be difficult to distinguish from other commonly seen psychiatric and neurological disorders. It is caused by a CGG repeat expansion in the premutation range (55-200) in the fragile X mental retardation 1 gene (FMR1)1. The premutation is present in 1/813 men and 1/259 women in the general population2,3. Carriers were initially thought to be free of phenotypic effects; however, male carriers are now known to be at risk of developing FXTAS from their 50s with an estimated 75% affected in their 80s4,5.

The most prominent clinical features include gait ataxia, intention tremor, short-term memory loss, executive dysfunction and behavioural difficulties. Evidence suggests that male carriers may have a six fold increased risk of developing cognitive decline. Cognitive impairment may precede any motor symptoms and may be the only presenting complaint6 and some patients may progress to dementia7. Parkinsonism, peripheral neuropathy, lower-limb muscle weakness, and autonomic dysfunction including urinary and bowel incontinence have also been described8. MRI typically shows cortical atrophy, ventricular enlargement and patchy white matter lesions in the cerebral hemispheres and middle cerebellar peduncles9.

Core features included:
- Apathy and Self Neglect. Neglecting personal care and socially withdrawing. The house was uncle, in disarray, with dog faeces and urine on the floor. Appeared indifferent while his wife had a hypoglycaemic attack.
- Cognitive impairment. Antegrade memory difficulties. He forgot his PIN number. He left the cooker on resulting in a fire. Misplacing items, accusing stepson of stealing them.
- Poor planning and impaired judgement

Locked三位一体 in hotel room 2 years prior to go out sightseeing, although aware she has dementia, her memory is independent. He wished to take her on holiday again. He fed her cat food and repeatedly took her upstairs despite her being bedbound. He used a camping stove inside the house and was caught by the motorway driving on flat tyres. He invited sales people into his home whom he believed he had promised him money.
- Disinhibition and behavioural disturbance

Mated sexuall inappropriate and racist remarks towards his wife’s carer. Aggressive and violent, hitting out when frustrated. He was setting fire to items of furniture in the garden.

No symptoms of depression and psychosis. He continued to have falls. There was one episode of lower limb weakness whilst bathing which required paramedic assistance.


Medication: simvastatin 20mg OD.

Social, Personal History, Premorbid Personality and Family History
Born in Watford. He described an unhappy childhood and did poorly at school, infrequently attending. He left age 16 with no high school qualification and worked in a shop, then as a milkman until age 65. He married 3 times and had 3 daughters by his 1st and 2nd wife. He lives with his 3rd wife of 30 years, her son and his partner. He was an active man who liked gardening. He always held racist beliefs and some patients may progress to dementia. He was ataxic which had been diagnosed as cerebellar syndrome of unknown cause with signs of possible normal pressure hydrocephalus (NPH) on MRI. He underwent a period of assessment in 2012.

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Management & Progress
Initially carbamazepine and later sodium valproate were initiated to aid in the management of his erratic mood swings and aggressive behaviour. Carbamazepine was stopped due to GP concerns regarding interaction with simvastatin. Sodium valproate was stopped owing to little benefit. A Community Psychiatric Nurse (CPN) was assigned to monitor mental and physical function and behaviour. As behaviour deteriorated a greater degree of intervention was required. His family had difficulty accepting his bizarre behaviour and paranoia, tending to inflame rather than deescalate any situation. This was managed through continuous psycho-education and support to his family and wife's carers. The CPN encouraged him to manage his self-care. An Occupational Therapist introduced aids to support Mr F's deteriorating mobility.

A case conference was organised involving representatives from his wife’s carer’s company, social services and the HFT. The outcome was a planned capacity assessment to determine his ability to decide on future care and accommodation. We plan to commence a selective serotonin reuptake inhibitor which has evidence of benefit in patients with disinhibition, emotionalism and dysexecutive function.

Discussion
We describe a case presenting to psychiatry with symptoms in keeping with FXTAS, confirmed with imaging and genetic testing. FXTAS is the most common known single-gene form of tremor and ataxia, and possibly of dementia, in older adults. It is a recently described syndrome with a variable presentation so diagnosis may be missed. Cognitive impairment may be the only presenting complaint. It is therefore important for clinicians working with an older population and in memory clinics to be aware of the syndrome to diagnose and manage, educate the family and offer genetic counselling where indicated. The pattern of cognitive decline in patients with FXTAS requires further longitudinal study. From this case, Mr F’s MMSE score declined by 2-3 points over 5 months. His behaviour also deteriorated. Further studies of helpful medications in FXTAS are warranted. To date, management is confined to symptomatic treatment. This can be limited given the nature and severity of risks accompanying the behavioural changes, cognitive decline, mobility problems and autonomic dysfunction, as in Mr F’s case. There have been no randomized controlled trials for treatment of the symptoms of FXTAS. Further prospective studies are required.