

# Dementia Prevalence Modelling

Michael Soljak, Kiara Chang, Maria Woringe

*Funded by Alzheimer's Research UK*

Alzheimer's  
Research UK  
Defeating Dementia

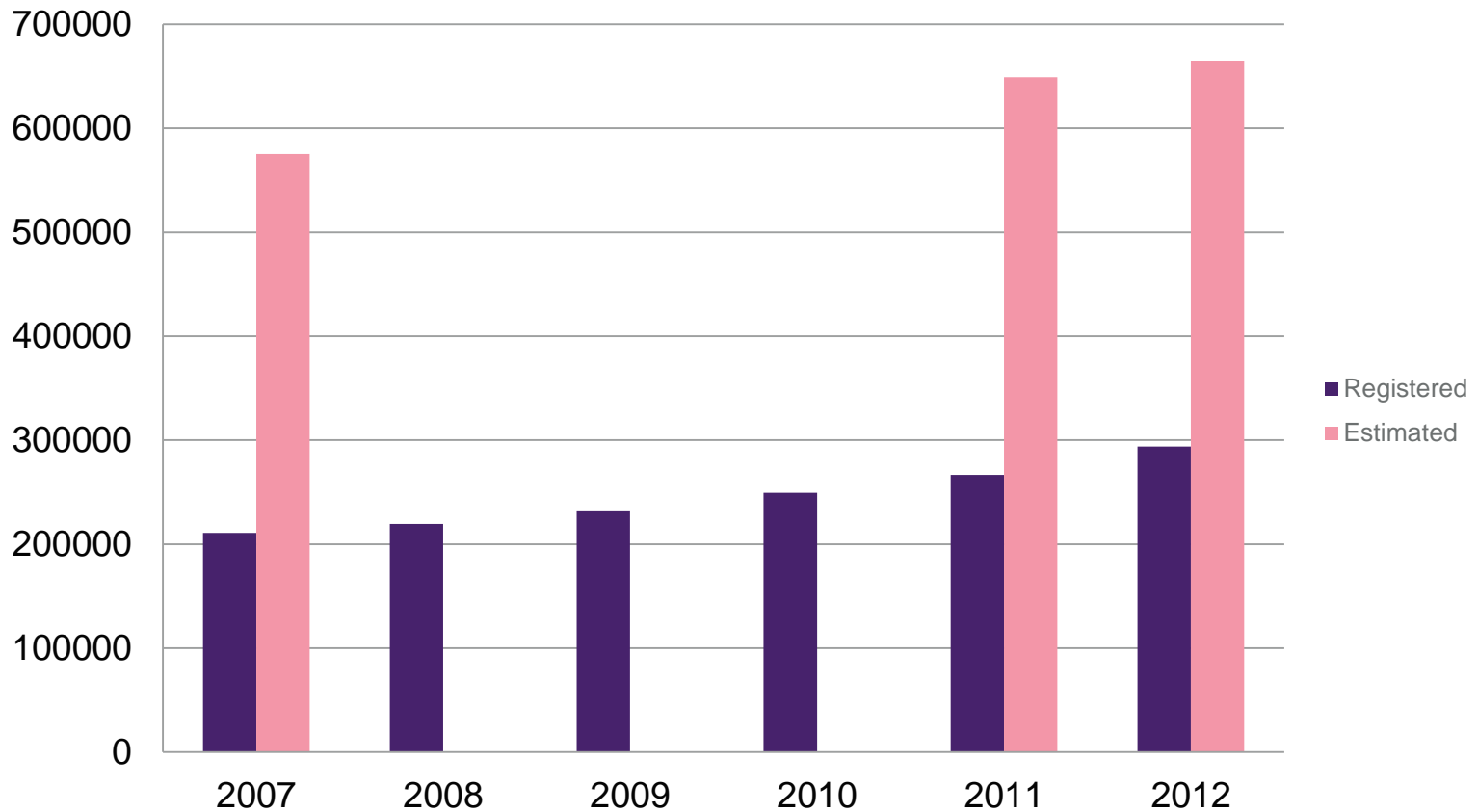
## Dementia Background

- 792,862 people living with dementia in the UK<sup>(1)</sup>
- 84% of dementia cases are in England<sup>(1)</sup>
- Less than half of the people with dementia receive a formal diagnosis <sup>(1)</sup>
- Dementia is more common in women than in men<sup>(1)</sup>
- Dementia costs £23 billion a year <sup>(2)</sup>
- Dementia affects around 5% of the over 65s, rising to 20% of the over 80s.<sup>(3)</sup>
- Number of dementia cases in the UK will double in 30 years and the national cost will be over £50 billion per year <sup>(4)</sup>

*Sources: Alzheimer's Society (2012) (1) "Dementia, A National Challenge" (2) "Mapping the Dementia Report 2012" ; (3) NICE COF Briefing Paper (2011) (4) UK National Dementia Strategy (2009)*



# GP Registered vs. Estimated Dementia Prevalence in England



Sources: Registered: QOF data. Estimated: Alzheimer's Society (2012) "Mapping the Dementia Report 2012", "2007 Dementia UK Report"

## Prime Minister's Challenge on Dementia

“We will ensure that GPs and other health professionals make patients aged 65 and older aware of memory clinics and refer those in need of assessment.

From April 2013, there will be a quantified ambition for diagnosis rates across the country, underpinned by robust and affordable local plans”



**Prime Minister, March 26 2012**

## Challenges to Screening

Open Letter to the BMJ 27.12.12

***Lack of evidence for the established criteria for screening such as availability of an effective treatment or intervention. Do the benefits outweigh any potential harm of screening?***

NICE Clinical Guideline 1.3.1.1 (2011)

***General population screening for dementia should not be undertaken.***

National Screening Committee (2010)

***Screening for Alzheimer's disease should not be offered.***

## Planned model development & project objectives

### Original Study Objectives

- Develop prevalence models for medium to high risk cognitive impairment and dementia
- Evaluate model performance
- Validate the models using an external data source
- Apply the models to the general practice and MLSOA populations

### Future Application

- Does targeted case-finding meet National Screening Committee criteria?

## Dementia Modelling

### Individual At Risk Modelling

- Model that predicts the risk of an outcome for an individual
- Most individual risk prediction models are poor at discriminating at risk individuals for dementia from non at risk cases.

### Population Prevalence Modelling

- Model that predicts the prevalence of an outcome in a given population
- Delphi Consensus
- Alzheimer's Society 2011-2012 Estimates
- Dementia Prevalence Calculator



## Background of English Longitudinal Study of Ageing (ELSA)

- Representative sample of people aged 50+ in England
- ELSA sample drawn from households responding to Health Survey for England (HSE) in 1998, 1999 and 2001
- ELSA wave 1 survey started in 2002, it is a longitudinal study with 4 waves (02'-03', 04'-05', 06'-07' 08'-09')
- Overall 16,624 people responded in 1 or more ELSA waves
- We chose 8,134 people whose age are 64+ (46% male, 98% white)
- 243 (2.98%) out of 8,134 people have self/proxy reported doctor diagnosed dementia, and 120 of the dementia cases were reported by proxy informant
- 42 (out of 8,134) people were interviewed in an institution (care home), and 41 of those have reported dementia

# Outcome measure in ELSA: self/proxy reported doctor-diagnosed dementia

Studies in literature use one of the criteria as the outcome “**Clinical dementia diagnostic**” : CAMDEX, ICD-10, DSM-IV and NINCDS

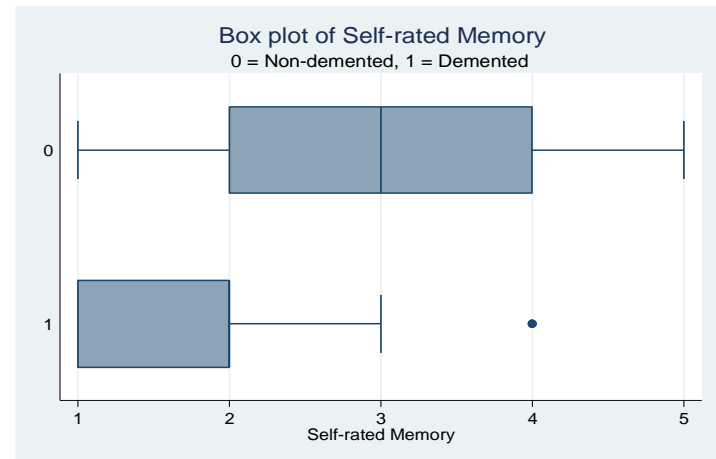
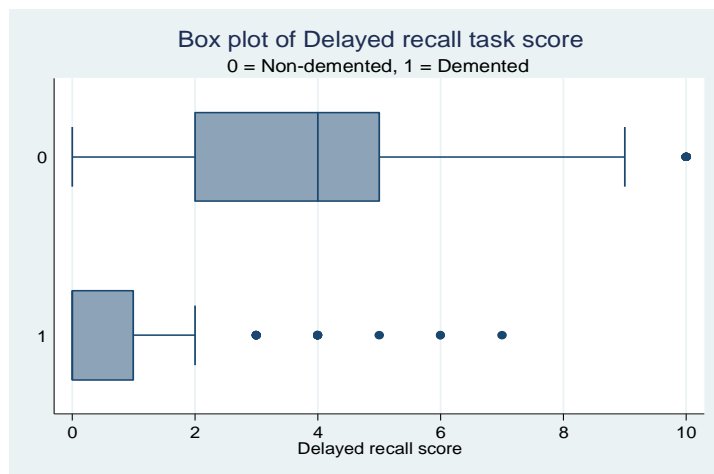
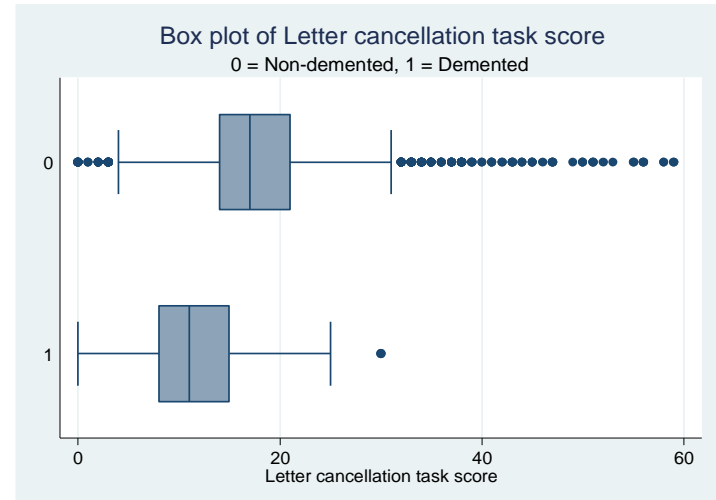
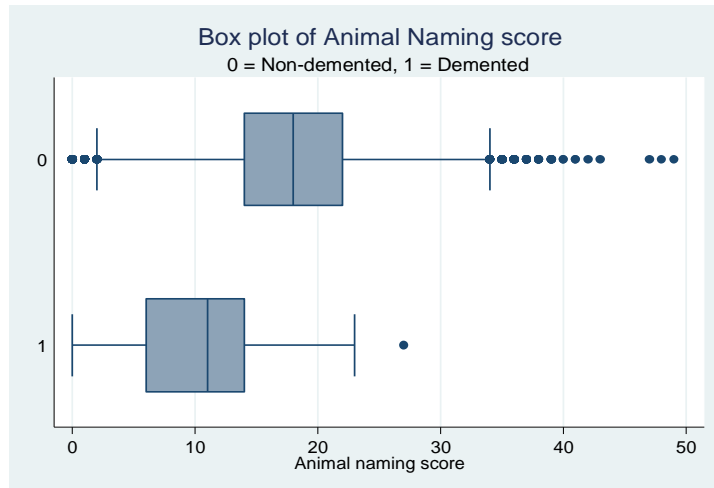
**DSM-IV** (Diagnostic and Statistical Manual of Mental Disorders)

## Diagnostic Criteria of Dementia

- **Memory impairment.** e.g. To recall the information after a delay of several minutes
- **Disturbances in executive functioning** - the ability to think abstractly and to plan, initiate, sequence, monitor. E.g. State as many animals as possible in 1 minute
- **Agnosia** - Failure to recognize or identify objects
- **Apraxia** - Impaired ability to execute motor activities. E.g. combing hair
- **Aphasia** - Deterioration of language function. E.g. To repeat phrases “no ifs, ands, or buts”
- **Memory impairment and cognitive function decline must be severe enough to cause a significant decline in social or occupational functioning and must show a decline from previous functioning**

# Outcome measure in ELSA: self/proxy reported doctor-diagnosed dementia

- DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) Diagnostic Criteria



1 = poor, 2 = fair, 3 = good, 4 = very good, 5 = excellent

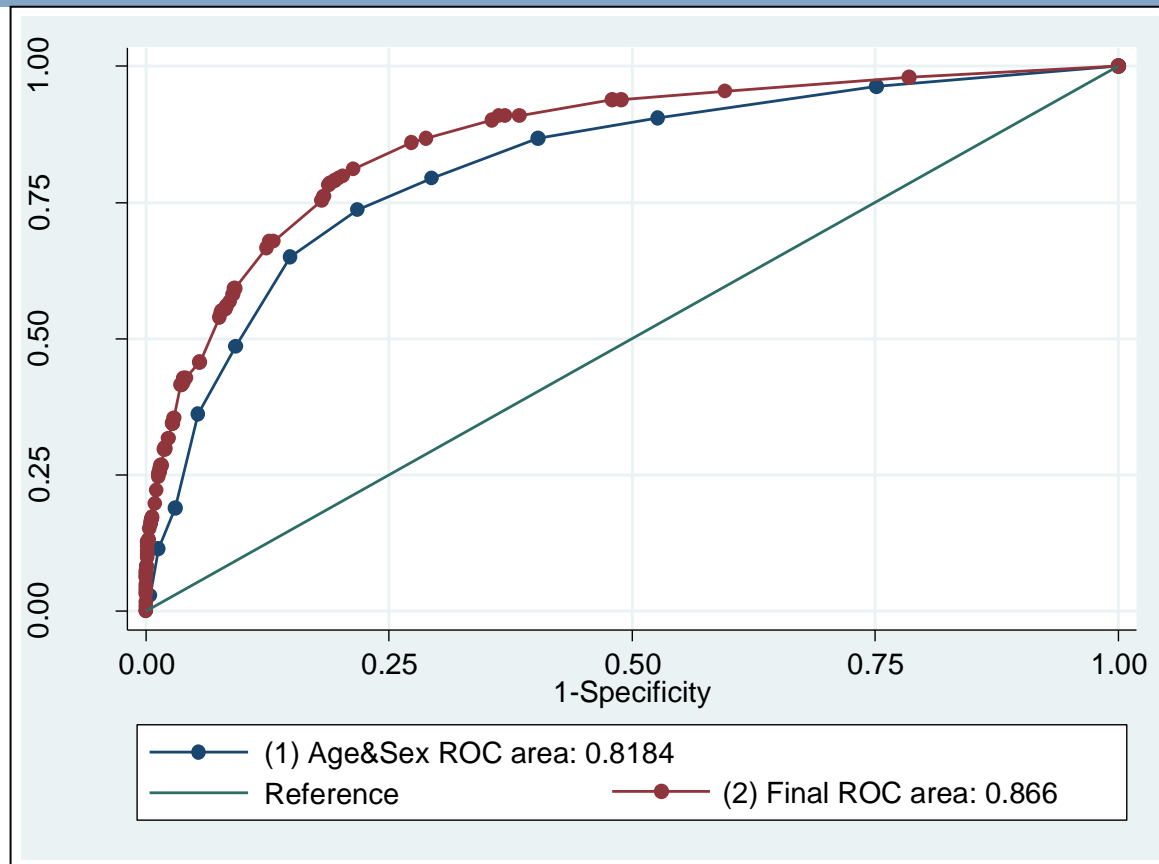
## Dementia model construction in ELSA

- **Covariates not used because missing too much**
  - Fruit intake, Total cholesterol, High density lipoprotein (HDL), HRT (only exist for women)
- **Covariates not used because not available locally**
  - Alcohol consumption, Parkinson's disease, self-rated memory
- **Other dropped covariates**
  - Ethnicity (99% white), Education (too many people have no qualification), Have any children
- **Covariates used:** age, gender, self-rated health, depression, smoking status, living with spouse, BMI, high blood pressure, diabetes, stroke, and NS-SEC8
- **Multiple imputation by chained equations (ICE)**
- **Uni-variate logistic regression**
- **Multi-variate logistic regression**

## Final ELSA Multivariate Model: Results

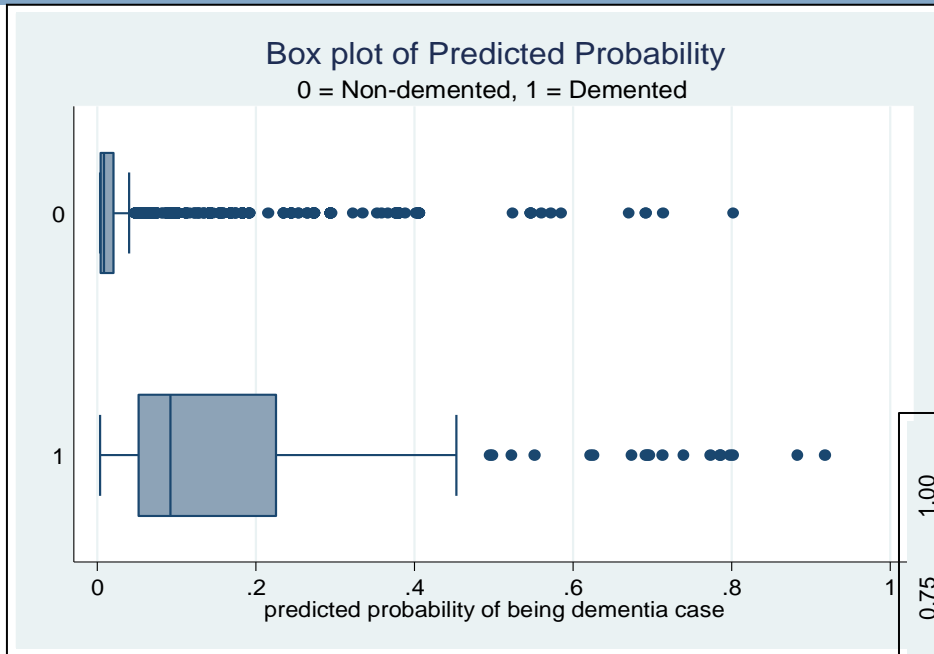
Variable	OR	p-value	95%CI	
Age(banded) 65-69	1.000			
70-74	2.577	0.001	1.454	4.569
75-79	5.715	0.000	3.294	9.917
80-84	16.418	0.000	9.935	27.130
85-89	30.576	0.000	18.048	51.799
90+	50.042	0.000	26.782	93.504
Female	0.900	0.478	0.675	1.202
Depression	5.971	0.000	3.025	11.788
Diabetes	3.032	0.000	1.899	4.840
Stroke	3.707	0.000	2.615	5.255

# Model Assessment in ELSA: Is Our Final Model Better than Age & Sex only Model?



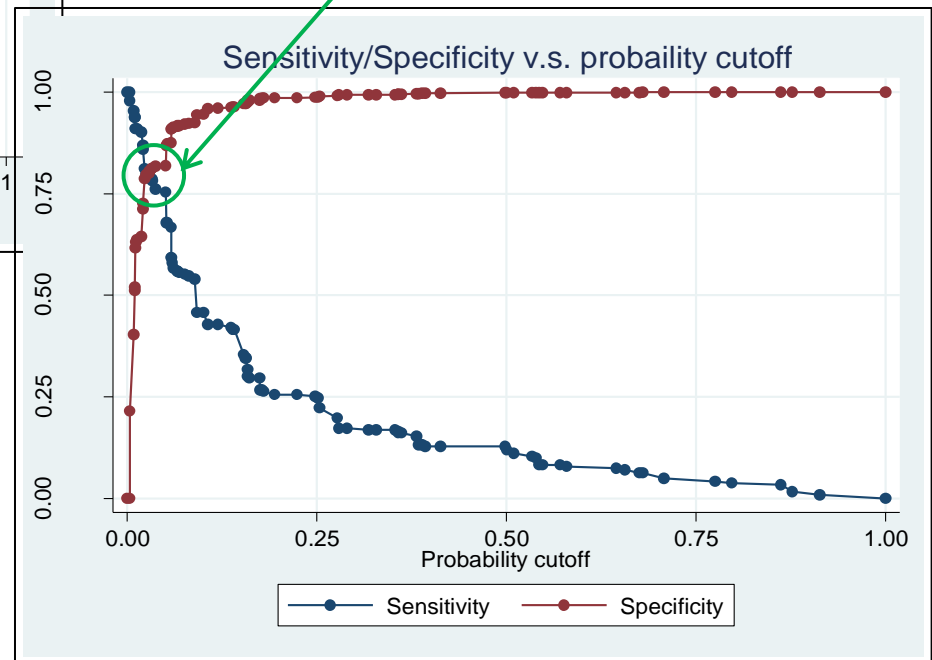
ROC comparison		AUC	S.E.	95% CI		Prob>chi2
Model 1	Age&Sex	0.8184	0.014	0.791	0.845	0.0000
Model 2	Final	0.8660	0.012	0.842	0.889	

# Model diagnostic in ELSA: How well does the model predict the data?



Probability cut-off = 0.025  
Sensitivity = 79.84%  
Specificity = 79.64%

Sensitivity =  $\Pr(+ve | \text{case})$   
Specificity =  $\Pr(-ve | \text{non-case})$



## Model diagnostic in ELSA: How well does the model predict the data?

Compare dementia casesness	ELSA Reported dementia	ELSA Non-demented	Total
Predicted demented	198	1607	1805
Predicted non-demented	45	6284	6329
Total	243	7891	8134

- Sensitivity =  $\Pr(+ve|case) = 198/243 = 81.4\%$
- Specificity =  $\Pr(-ve | non-case) = 6284/7891 = 79.6\%$
- This coincides with what we expected to get
- The AUC for this model is 0.8660 (0.842, 0.889)
- This multi-variate model has done well in predicting the outcome



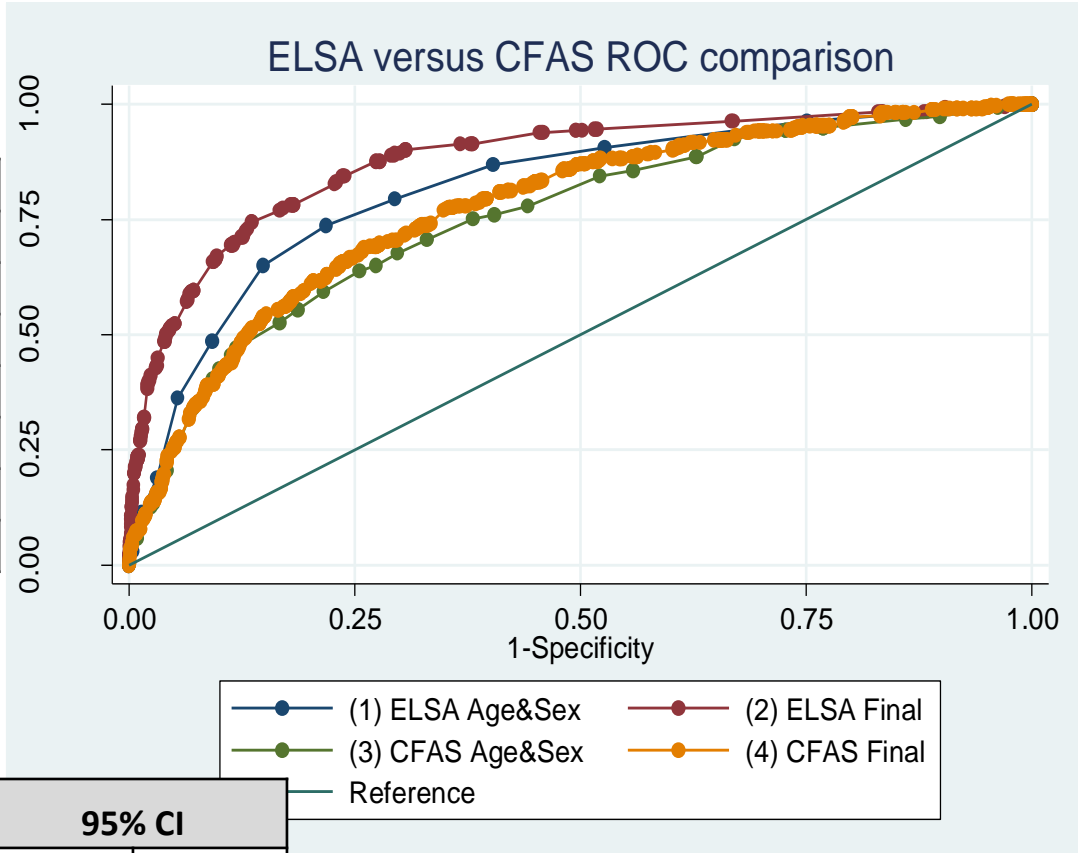
## External comparison: ELSA vs. CFAS

List	ELSA (2002-2009)	CFAS(1991-1997)
Population	England 64+	England & Wales 65+
Waves	1 to 4	2 & 3
No. demented	243	277
Controls	7891	3800
Education	25% A level+	36% 10 years+
Ethnicity	99% White	73% White
Institutionalized	42(0.52%)	710(5.6%)
Dementia definition	Self reported doctor diagnosed	No diagnosis, GMS & AGE-CAT algorithm(score 3-5)

*CFAS = Cognitive Function Study of Ageing*

## External comparison: ELSA vs. CFAS

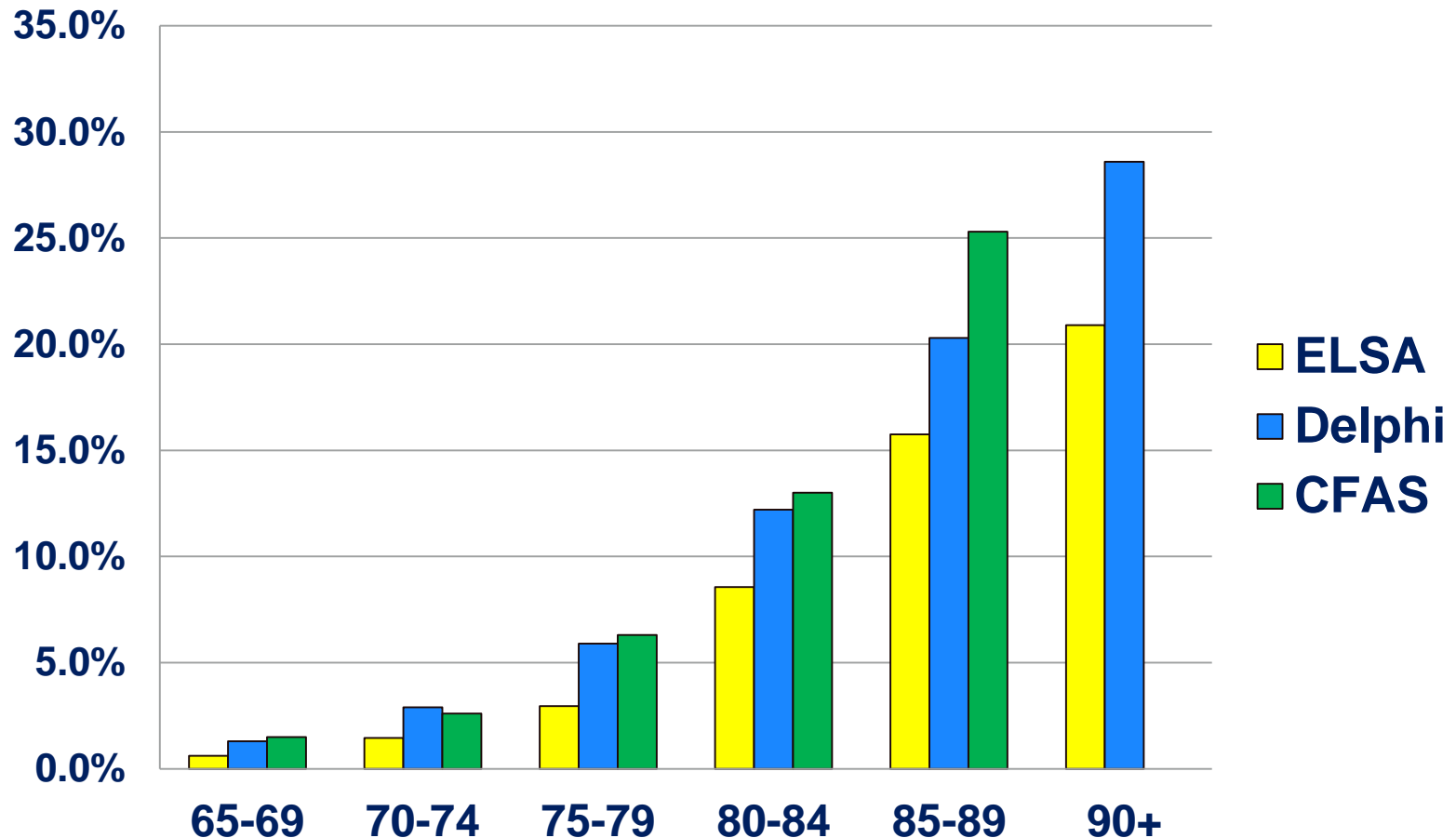
ELSA Final 5 Variables	CFAS Final 7 Variables
Age	Age
Sex	Sex
Depression	Wave
Diabetes	Education
Stroke	Self-rated health
	Stroke
	Live in institution



Model	Specification	AUC	Std. Err.	95% CI	
1	ELSA Age&Sex	0.8184	0.0140	0.7910	0.8458
2	ELSA Final	0.8792	0.0121	0.8554	0.9030
3	CFAS Age&Sex	0.7541	0.0141	0.7265	0.7820
4	CFAS Final	0.7759	0.0132	0.7499	0.8020

## How Do Our Findings Compare with the Literature?

**Prevalence of Dementia According to ELSA, Delphi Consensus (2007) and MRC CFAS (1998)**



## Consistencies with the Literature

- Strong systematic review evidence of diabetes, depression and stroke being predictive of dementia.
- ELSA OR were significantly higher than the pooled odds ratios reported in systematic reviews
  - Diabetes OR=1.5<sup>(1)</sup>
  - Diabetes OR=3.03 (1.89-4.84) in ELSA
  - Depression OR = 2.30 (1.71-3.09) with diagnostic dementia criteria, OR=1.91 (1.62-2.26) without <sup>(2)</sup>
    - Depression OR=4.57 (1.03-1.85) 1 year before onset of AD; OR=1.71 (1.03-2.82) >25 yrs before onset of AD <sup>(3)</sup> in a study not using formal criteria for dementia & depression
  - Depression OR=5.97 (3.03, 11.79) in ELSA
  - Stroke OR=2.0 <sup>(4)</sup>
  - Stroke OR=2.2 (1.6-3.0) with previous stroke, OR=1.7 (1.1-2.5) w/ multiple strokes <sup>(5)</sup>
  - Stroke OR = 3.71 (2.62, 5.26) in ELSA

*References: (1) Kloppenborg et al(2008); (2) Ownby RL (2006); (3) Green RC (2003); (4) Savva (2010) et al; (5) Pendlebury ST (2009)*

## Inconsistencies with the Literature

- Sex was not significant
- Living with spouse was found to be a significant risk factor for dementia
- Self-rated health was significant univariately but not in a multi-variate model
- While current smoking was not significant, ex-smoking adjusted by age and gender was a significant protective factor in ELSA

## Conclusions / Recommendations

- ELSA model over predicts dementia in over 65s (20% vs. patient / proxy reported 3%)
- ELSA model correctly identifies 80% of reported dementia cases and 80% of non-demented cases
- Does the combined risk factor profile of depression, diabetes, and stroke helps to identify more dementia cases in over 65 at the GP level?
- Option 1: Apply the model to all local population data and disseminate our findings via DH
- Option 2: Apply the model to selected local populations for targeted case-finding R&D study