

Outline

- methodology of surveys
 - range of prevalence for autism for related disorders
 - other correlates : medical disorders, ethnicity..
 - time trends
 - cluster reports
 - USA estimates : N of persons with a PDD

Autism : study selection

- English language journals
- 32 surveys from 1966 to 2001
- 13 countries
- median age : 8.0 years (*birth to adult life*)
- population size : median : 66,000
range : 826 - 900,000

Autism Surveys : Methodology

Screening stage

- letters, brief scales or checklists, ...
- informants: teachers, paediatricians, speech therapist, service providers,...
- variable coverage:
 - medical / educational records,
 - special schools, well-baby clinics,
 - mainstream schools, private clinicians
- good participation
- unknown sensitivity

Autism Surveys : Methodology

Diagnostic stage

- case definition : Kanner criteria 1960s
 - Rutter criteria/ICD-9 1970s
 - DSM-III and III-R 1980s
 - DSM-IV and ICD-10 1990s

- assessment procedures:
 - . review of records
 - . direct assessment of child
 - CARS, ABC, ADI-R

- final caseness determination using judgement of clinical experts

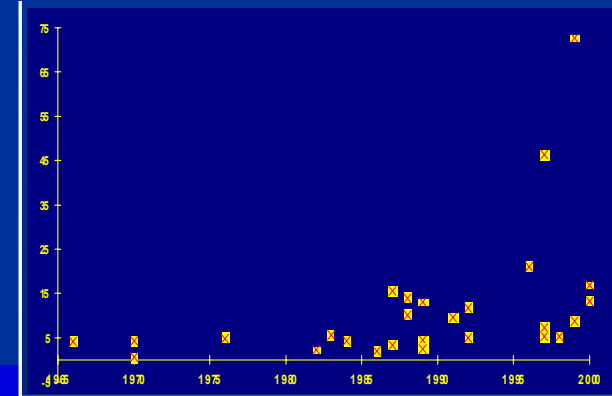
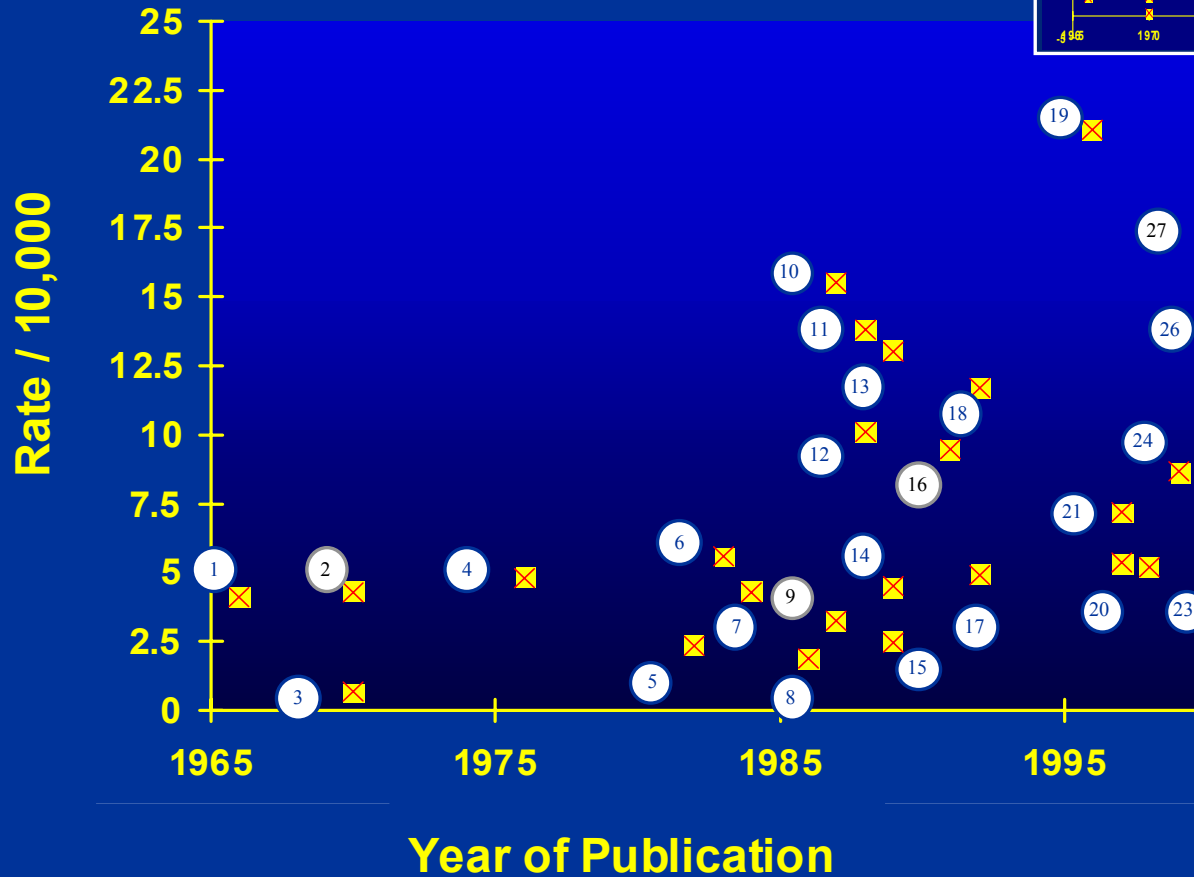
Autism Surveys : Sample characteristics

N with autism	: 2,380 in 32 surveys median = 50 per survey
Positive predictive value (PPV) of screens	: 33%
Intellectual level	: normal : 30% mild - moderate MR : 30% severe - profound MR : 40%
Sex ratio (M / F)	: 4.2 to 1 lower if more retarded

Autism Surveys : Prevalence estimates

- ◆ median : 8.7 / 10,000 (range : 0.7 - 72.6)
- ◆ average width 95% CI : 12.0 (range : 0.3 - 115.9)
- ◆ prevalence rates correlate with
 - sample size : $r = -.77$ (*Spearman; p < .01*)
 - publication year : $r = .70$ (*Spearman; p < .01*)
- ◆ about equal subdivision in typical and atypical forms

Prevalence of autism in 27 surveys



Best estimate for AD prevalence

- exclude studies with low precision

i.e. target N < 10,000

- focus on recent surveys

mean median

since 1989 (15 surveys)

11.2

8.7

since 1987 (19 surveys)

11.1

9.5

- best conservative estimate : 10 / 10,000

Relative rates of AD and PDD NOS

<u>Study</u>	<u>Definition for other PDD</u>	<u>AD</u>	<u>PDD NOS</u>	<u>Ratio</u>
Lotter (1966)	behaviour similar to autistic children	4.1	3.3	0.8
Brask (1970)	'other psychoses' or 'borderline psychotic'	4.3	1.9	0.4
Wing et al (1976)	socially impaired <i>(triad of impairments)</i>	4.9	16.3	3.3
Hoshino et al (1982)	autistic mental retardation	2.3	2.9	1.3
Burd et al (1987)	'autistic-like'	3.3	> 7.8	2.4
Cialdella & Marmelle (1989)	other forms of 'infantile psychosis'	4.5	4.7	1.0

Relative rates of AD and PDD NOS

<u>Study</u>	<u>Definition for other PDD</u>	<u>AD</u>	<u>PDD NOS</u>	<u>Ratio</u>
Fombonne & Mazaubrun (1992)	other PDDs	4.6	6.6	1.4
Fombonne et al (1997)	other PDDs	5.3	10.9	2.1
Powell et al. (2000)	autism-spectrum disorders	7.8	13.0	1.7
CDC (2000)	PDD NOS	40	27.0	0.7
Baird et al (2000)	PDD NOS	27.7	27.1	1.0
Chakrabarti & Fombonne (2001)	PDD NOS	16.8	36.1	2.1

Childhood disintegrative disorder (CDD)

	N	M/F	Prevalence estimate (/10,000)	95% CI ¹ (/10,000)
Burd et al., 1987	2	2/0	.111	.013; .399
Sponheim & Skjeldal, 1998	1	?	.152	.004; .848
Magn. & Sæm., 2001				
1974-93	2	2/0	.234	.028; .844
1964-73 ²	4	3/1	.311	.085; .795
Chakrabarti & Fombonne 2001	1	1/0	.645	.016; 3.59

¹ : 95% CI derive from exact binomial calculations

² : data from Magnusson (1977)

Surveys of Asperger syndrome

- Ehlers & Gillberg, 1993
 - 5 Swedish normal schools
 - 1519 children aged 7 to 16
 - 4 definite cases (ICD-10)
 - prevalence : 28.5/10,000 (95% CI = 0.6 - 56.5)

- Kadesjö et al., 1999
 - 826 children aged 7
 - 4 boys
 - prevalence : 48.4/10,000 (95% CI = 1.1 - 95.8)

Asperger syndrome in recent autism surveys

	Autism		AS		Autism / AS Ratio
	Prevalence	N	Prevalence	N	
Sponheim & Skjeldal, 1998	4.9	32	.3	2	16.0
Taylor et al., 1999	8.7	427	1.4	71	6.0
Kadesjö et al., 1999	72.6	6	48.4	4	1.5
Powell et al. 2000	-	54	-	16	3.0
Baird et al. 2000	27.7	45	3.1	5	9.0
Chakrabarti & Fombonne 2001	16.8	26	8.4	13	2.0

Overall

163

40

4.1

excluding Taylor et al.

Estimates deriving from the review

Autistic disorder	10.0 / 10,000
Asperger syndrome	2.5 / 10,000
PDD NOS	15.0 / 10,000
All PDDs	27.5 / 10,000

Newer surveys

	Age	Autism			PDDNOS + AS			All PDD
		rate / 10,000	M / F ratio	% IQ normal	rate / 10,000	M / F ratio	% IQ normal	rate / 10,000
CDC, 2000	3-10	40.5	2.2	37	27.0	3.7	51	67.5
Baird et al, 2000	7	30.8	15.7	60	27.1	4.5	-	57.9
Chakrabarti & Fombonne 2001	4-7	16.8	3.3	29	44.5	4.3	94	61.3



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Autism Surveys : Medical conditions %

	<u>Median rate</u>	<u>Range</u>
Cerebral palsy	2.0	0 - 4.8
Fragile X	0.3	0 - 8.1
Tuberous sclerosis	1.2	0 - 3.8
PKU	0	0 - 0
Neurofibromatosis	0	0 - 1.4
Congenital rubella	0.3	0 - 5.9
Down's syndrome	1.3	0 - 16.7
Any of the above	6.4	0 - 16.7
Epilepsy	16.8	0 - 26.4
Hearing impairments	1.7	0 - 5.9
Visual impairments	1.3	0 - 11.1

PS: no report of measles encephalitis or SSPE

Autism Surveys : Other findings

- no association with social class in post 1980 surveys
- association with immigrant status or ethnicity : largely unsupported
- geographical variation in prevalence
 - * methodological variation between studies confounds comparisons
 - * limited evidence not in favour of between-countries variations in rates.

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Time trends in autism

- Problems :
 - prevalence versus incidence rates
 - secular changes in age at diagnosis
 - statistical power issues
 - changes in case definition / case finding

		case	not case	
screen	+	50	100	150
	-	?		
		?		100,000

prevalence = $50 / 100,000$

“true” prevalence = ?

Time trends in autism

- comparison of prevalence surveys over time
- referral statistics
- repeat surveys in defined areas
- trends in rates in consecutive birth cohorts
- incidence studies

Study design impact on prevalence

Example of 4 recent UK surveys

	<u>location</u>	<u>size</u>	<u>age group</u>	<u>method</u>	<u>PDD rate</u> <u>/10,000</u>
Baird et al. 2000	South.East Thames	16,235	7	Early screening + FU identification	57.9
Chakrabarti & Fombonne 2001	Stafford -shire	15,500	2½ - 6½	intense screening + assessment	62.6
Fombonne et al. 2001	England & Wales	10,438	5 - 15	household survey	26.1
Taylor et al. 1999	North Thames	490,000	0 - 16	administrative records	10.1

Six-fold variation in estimates



Study design impact on prevalence

Example of 4 recent US studies

	<u>location</u>	<u>size</u>	<u>age group</u>	<u>method</u>	<u>PDD rate</u> <u>/10,000</u>
CDC, 2000	Brick Township NJ	8896	3-10	multiple sources of ascertainment	67
CDER, 1999	California	3,215,000	4 - 9	educational services	15
Sturmey, 2001	Texas	3,564,577	6 - 18	educational services	16
Hillman et al., 2000	Missouri	-	5 - 9	educational services	4.8

idem



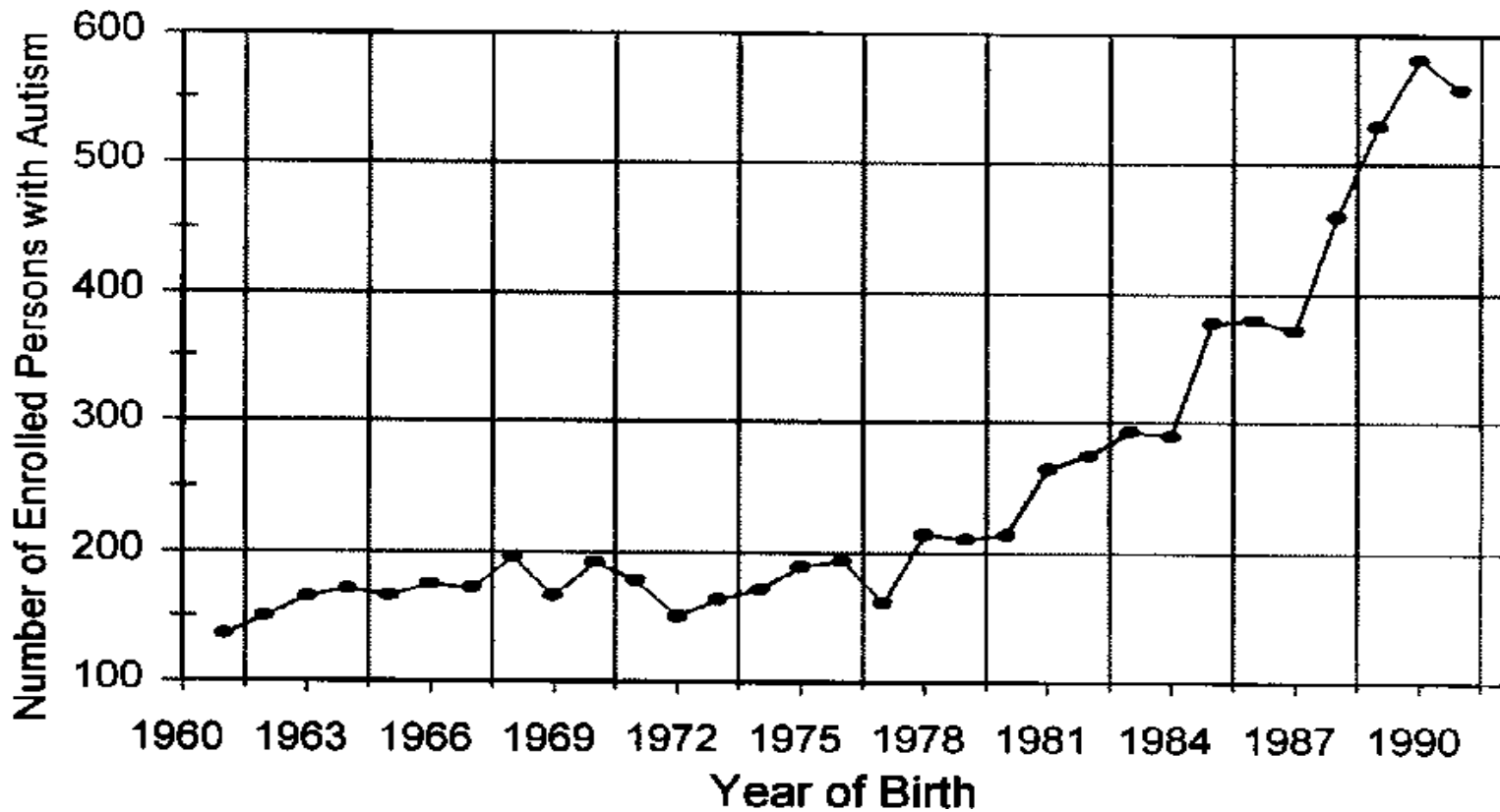
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California CDER data (1987-1998)

	<u>1987</u>	<u>1998</u>	<u>% change</u>
Autism <i>(full syndrome or residual state)</i>	2778	10360	+ 272.9 %
Other PDD	38	785	+1965.8 %
Autism suspected <i>(not diagnosed)</i>	1086	1635	+ 50.6 %

California CDER data : 1961 - 1991



California CDER report : problems

1. Numbers instead of rates

Californian population rose by 19.3% between 1987 and 1999 and by 25.8% for the 0 - 14 year olds

2. No control for changes in diagnostic practices

<u>< 1980</u>	<u>DSM-III</u>	<u>DSM-III-R</u>	<u>DSM-IV</u>
Infantile autism	PDD concept	PDD with low specificity	Asperger change in PDD-NOS (1 area instead of 2)

California CDER report : problems (cont'd)

3. Decreasing age at diagnosis
will produce ↗ in prevalence (assuming constant incidence)
4. No comparison with meaningful data
a PDD prevalence of 27.5/10 000 predicts 27 300 subjects
with PDD in California
5. Lack of specificity
upward trends reported for CD, epilepsy, MR
6. Distorted graphical display

Trends in rates : effect of decreasing age at diagnosis

Age	N	Time 1		Time 2	
		% diagnosed	N ₁	% diagnosed	N ₂
3	50,000	10	5	50	25
4	50,000	30	15	70	35
5	50,000	60	30	90	45
6	50,000	90	45	100	50
7	50,000	100	50	100	50


$\hat{P}_{3-7 \text{ year olds}}$

$$145/250,000 = 5.8$$

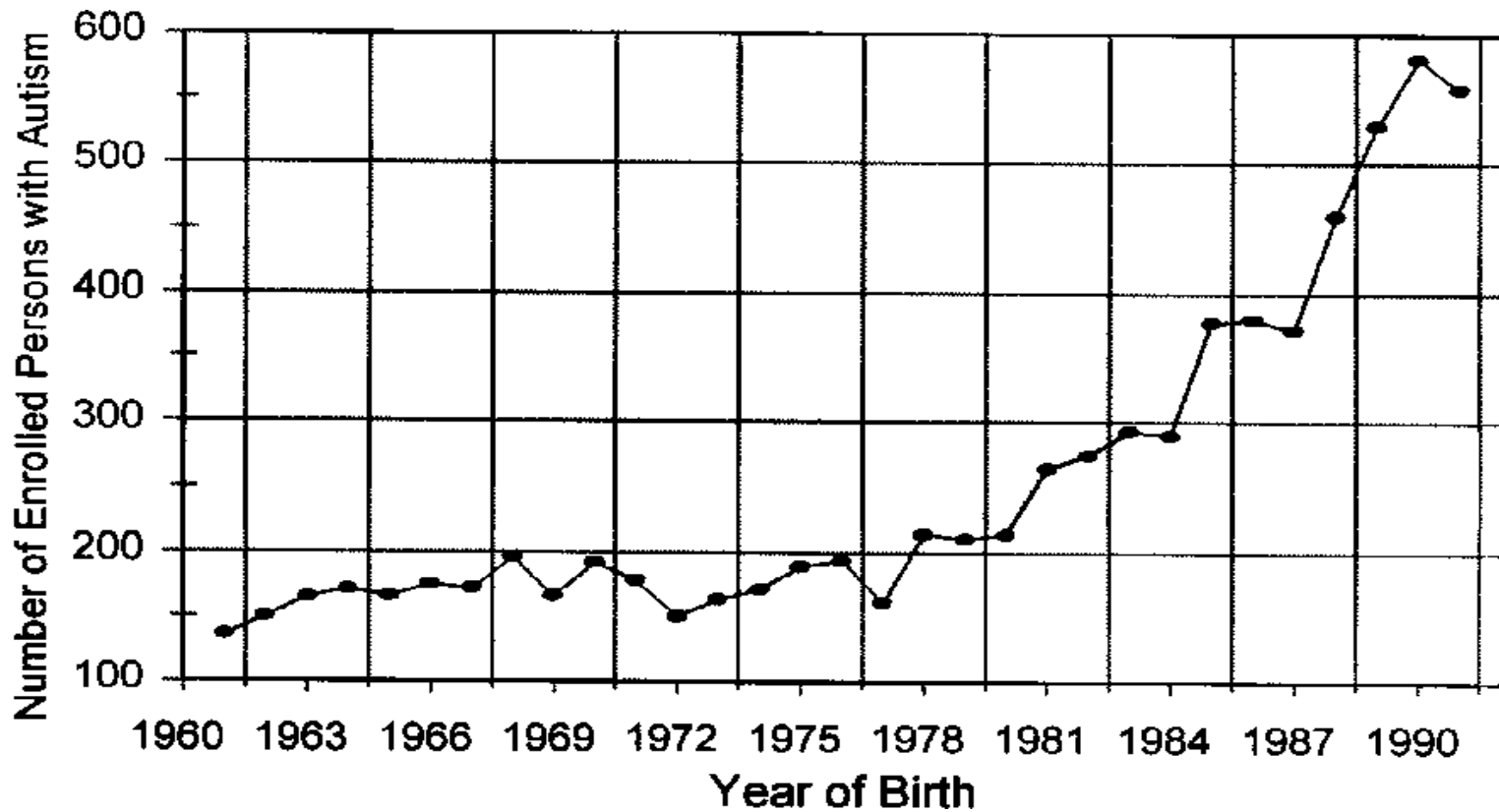
$$205/250,000 = 8.2 (+41\%)$$

Assumption : stable 'true' prevalence rate of 10/10,000

California CDER report : problems *(cont'd)*

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California CDER data : 1961 - 1991

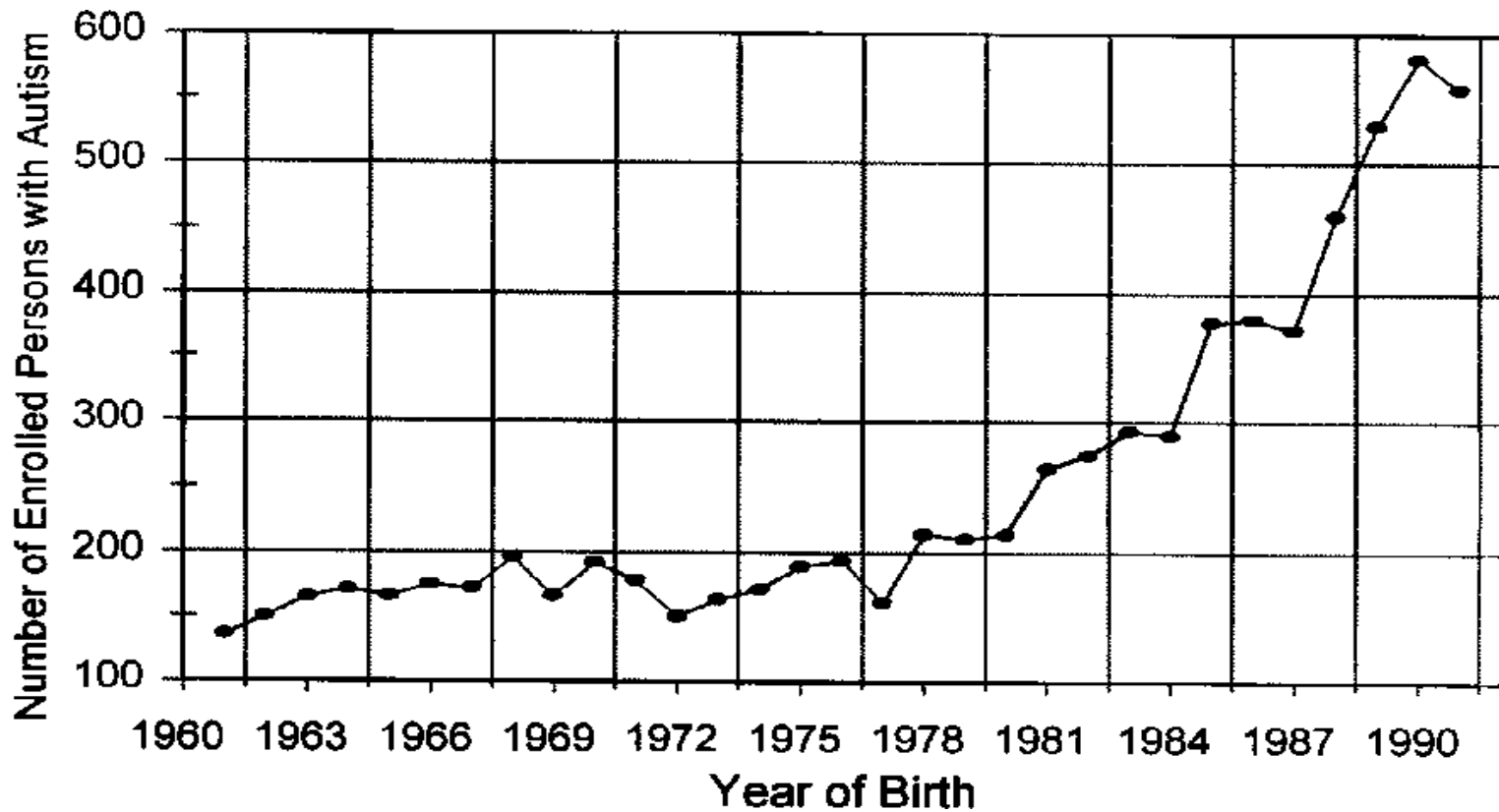


California CDER report

The Figure derives from the “ ... 1991 population of persons (7915) with autism”.

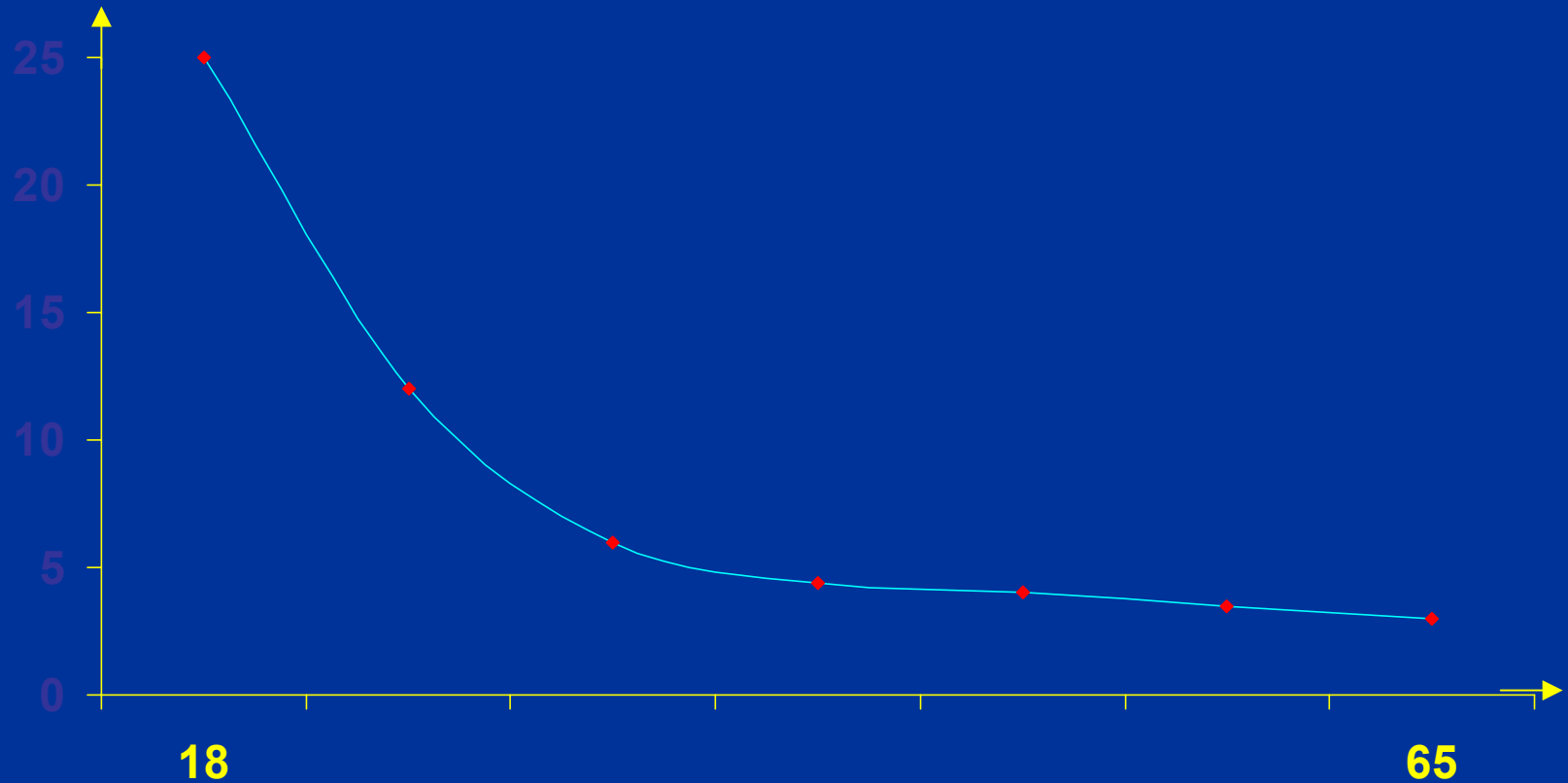
“Data points in Figure 1 do not show how many persons enter the system in a given year, but how many already in the system were born in a given year”

California CDER data : 1961 - 1991



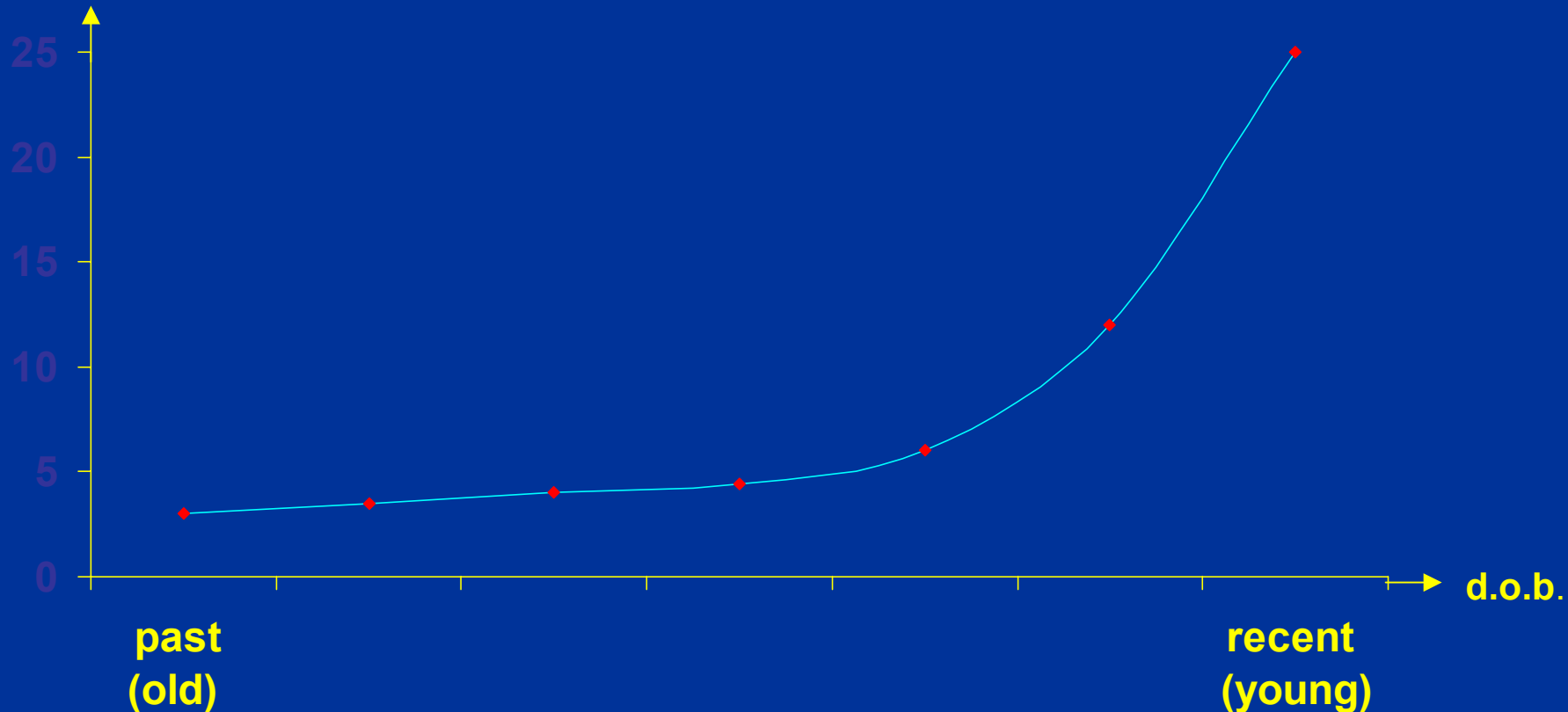
Army personnel : hypothetical survey

Age on X axis



Army personnel : hypothetical survey

Plotting date of birth (instead of age) on X axis



Time trends in autism

- comparison of prevalence surveys over time
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- trends in rates in consecutive birth cohorts
- incidence studies

Repeat surveys of autism

- Göteborg studies (*Gillberg et al., 1991*)

- Rates

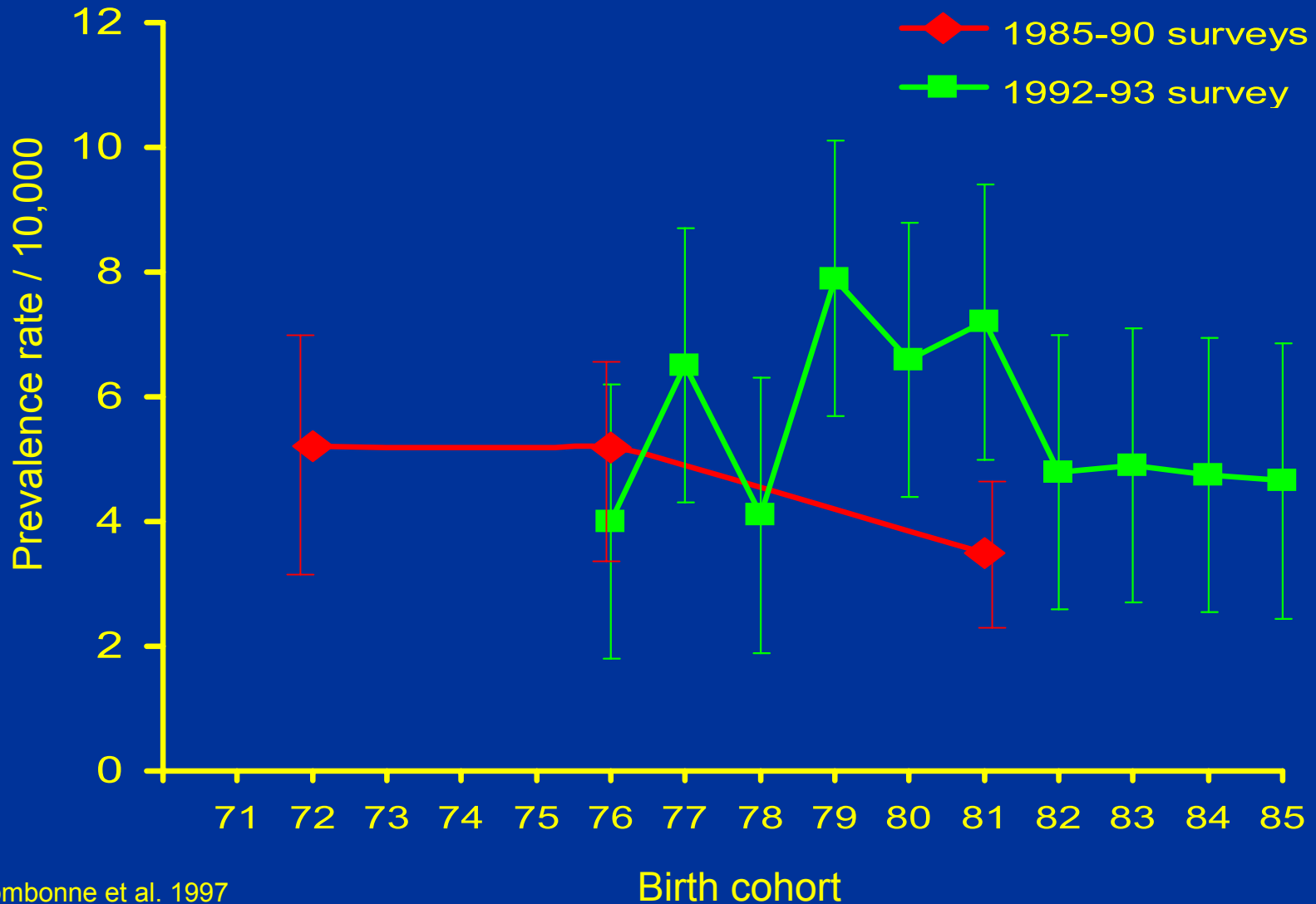
	<u>1980</u>	<u>1984</u>	<u>1988</u>
	4.0	6.6	9.5

- But : improved detection, changes in diagnostic concepts and definition, opening of a State Diagnostic Center, migration flux, etc. ...

Time trends in autism

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Prevalence rates by birth cohorts (1972-1985) in two surveys

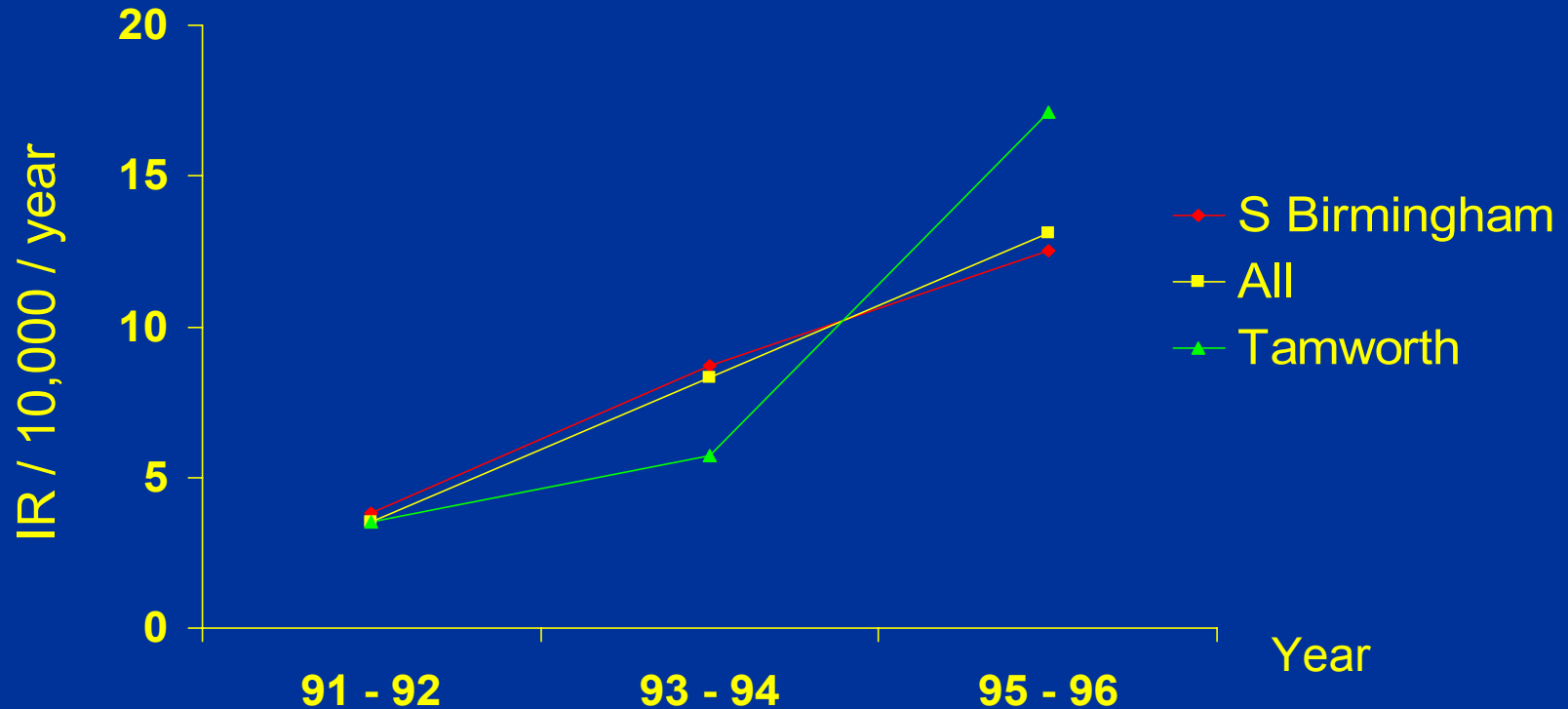


Time trends in autism

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Trends in incidence rates of ASD

West Midlands Study (N=148)

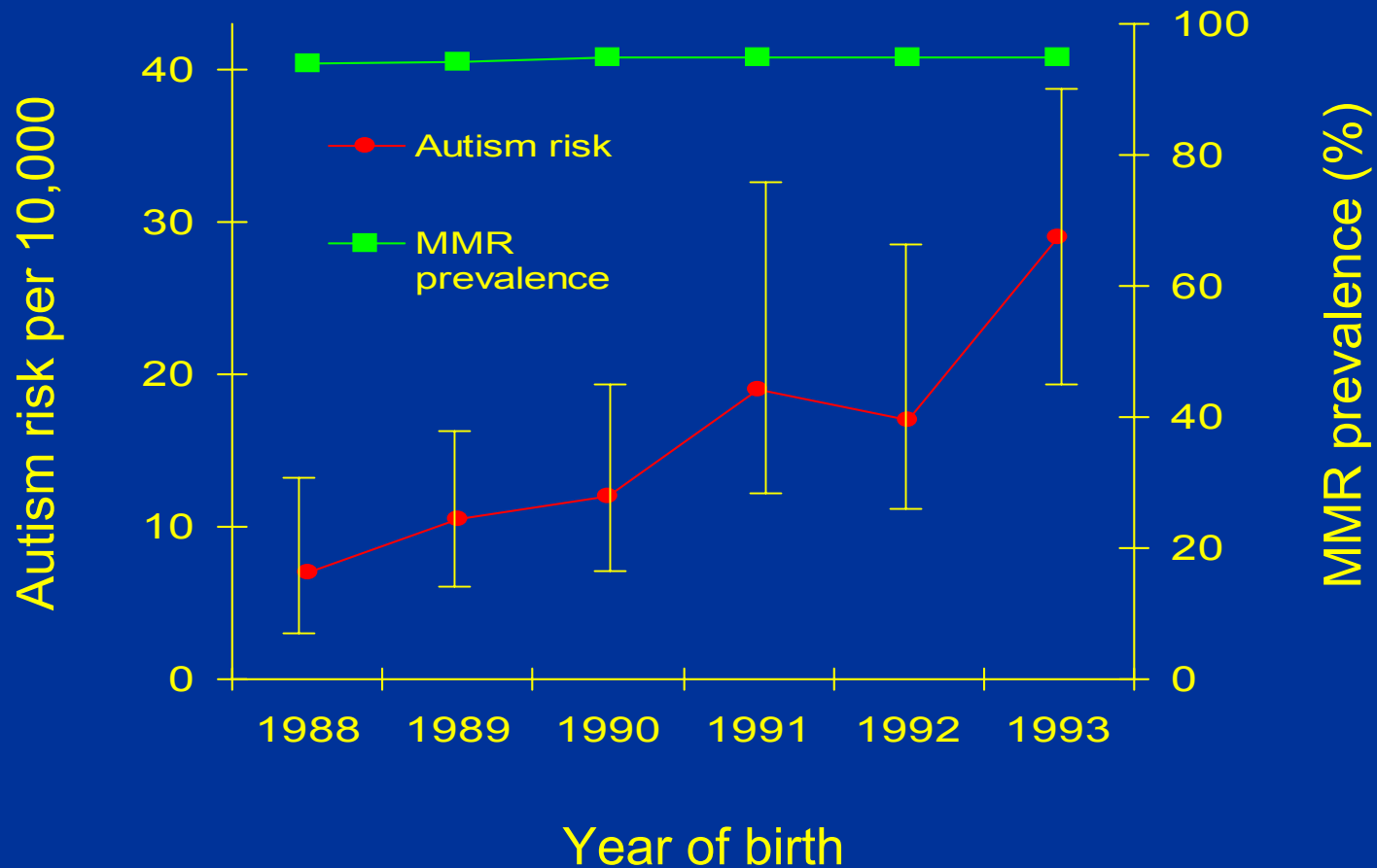


$IR_{\text{overall}} = 8.3/10,000/y$ (7.0 - 9.7)

annual increase rate ratio : 1.37 (1.24 - 1.52), $p < .001$

MMR coverage and autism risk

GP RD data



Time trends : conclusions

- Most studies are not informative to gauge trends over time
- Informative studies have generally failed to control for changes in case definition and case finding
- Prevalence rates have gone up but this trend cannot be interpreted as evidence of a secular increase in the incidence

Time trends : issues for future monitoring

- standardize survey methodology
 - case definition (PDD spectrum)
 - assessment tools (ADI-R, etc..)
- collect data at symptom level to allow for dimensional and categorical treatment
- focus on age group 8 - 12
- outcome measure : cumulative incidence
- assess correlates (i.e. IQ) for subgroup analyses
- sample size / power issues
- replication across several areas
- need for time- and space-clustering studies

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Baron-Cohen et al., 1999 EXAMPLE OF A RECENT CLUSTER IN STAFFORD, UK

Cluster reports

- pre-selection bias in cluster identification
 - ⇒ inappropriate comparisons between cluster and population incidence rates
- cluster reports require confirmation
 - focused tests of clustering at other suspected sources
 - post-alarm monitoring
 - space-time scan statistics
- if cluster confirmed, further epidemiological studies are needed

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USA estimates

	<u>Age groups</u>				<u>Under 18</u>
	<u>0-4</u>	<u>5-9</u>	<u>10 – 14</u>	<u>15 – 17</u>	
Autism	18,987	19,920	20,057	11,818	70,782
Asperger syndrome	4,747	4,980	5,014	2,955	17,696
PDD-NOS	28,481	29,880	30,086	17,727	106,173
All	52,214	54,780	55,157	32,500	194,650