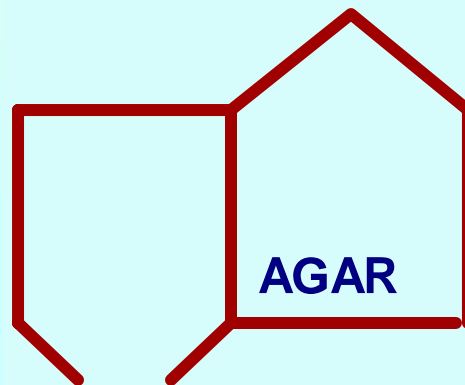


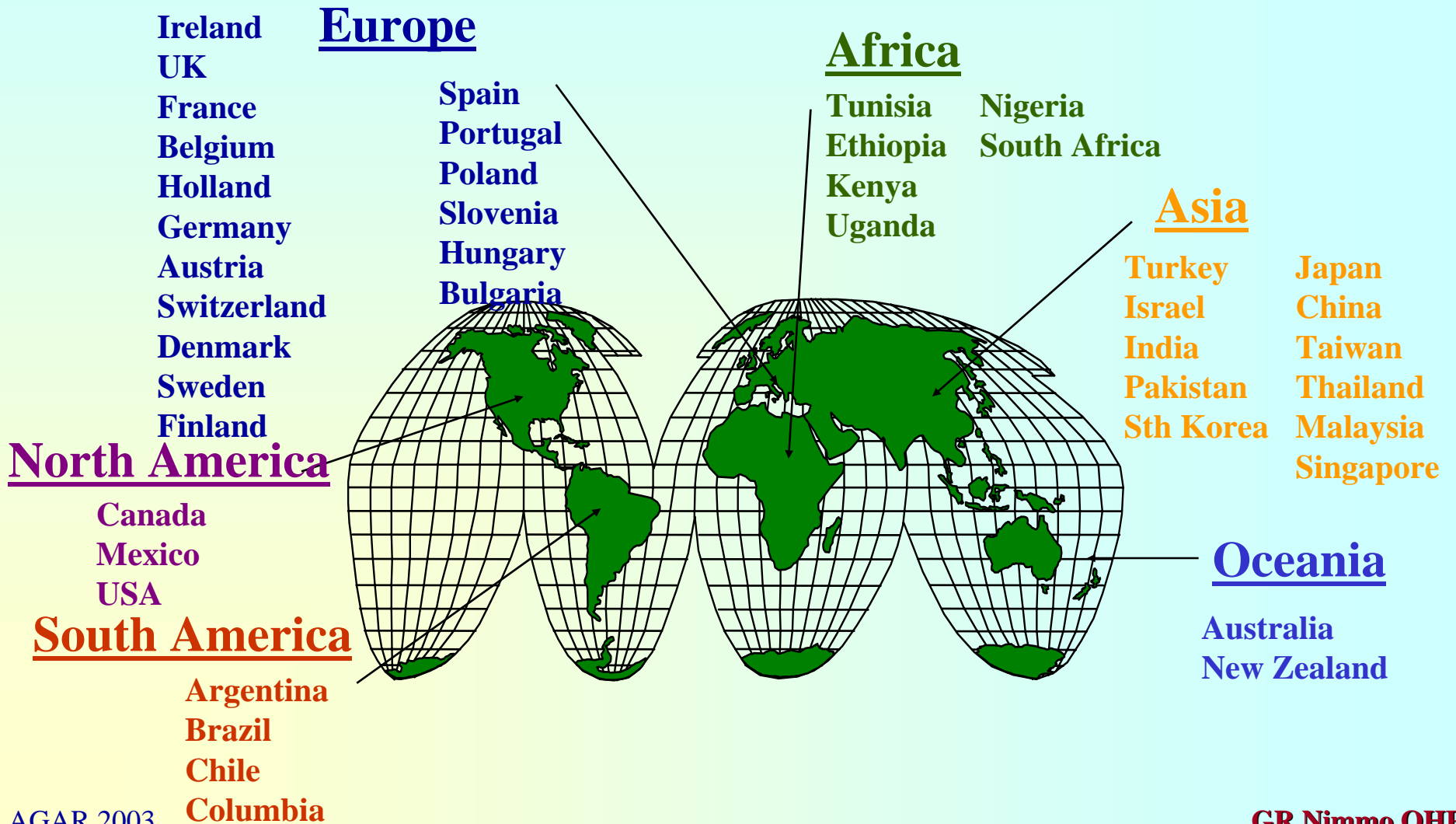
AUSTRALIAN GROUP FOR ANTIMICROBIAL RESISTANCE

Hospital MRSA Surveillance 1989-2001



Global Distribution of MRSA

- Reports in the literature 1988-2001



Historical Perspective

- Appeared soon after introduction of methicillin in 1960
- UK 1961 {Jeavons BMJ 1961;1:124-5.}
- Australia 1965 {Rountree & Beard MJA 1968; 2:1163-8.}
- Gentamicin resistant strains reported in 1976 in Australia {Perceval et al MJA 1976; 2:74.}
- Epidemic reported in late 1970s in Australia {Pavillard et al MJA 1982; 69:451-4}

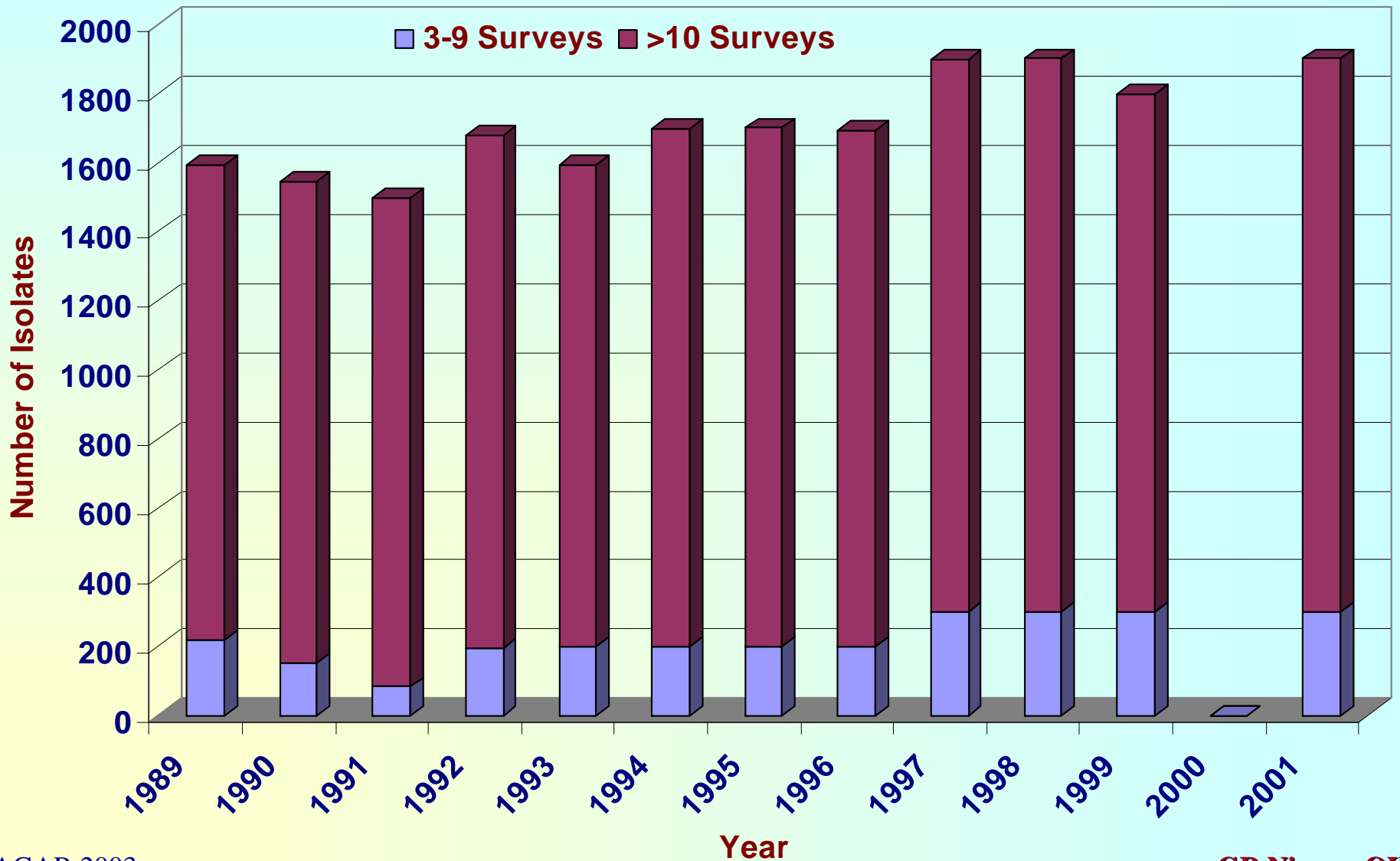
AGAR Staphylococcus aureus Survey

- Hospital surveys conducted since 1987
- Comparable data available for 1989-1999 and 2001
- Methods:
 - Approximately 100 consecutive clinical isolates (not ‘screening’), no repeats, each November
 - Teaching hospital laboratories in all capital
 - Agar dilution
 - Isosensitest + 5% HB, 1989-1992; NCCLS 1993 onwards
- Typing methods: phage typing (all) , coagulase PCR (2000-1), PFGE (2000-1), Ribotyping (2000), **MLST (2000)**

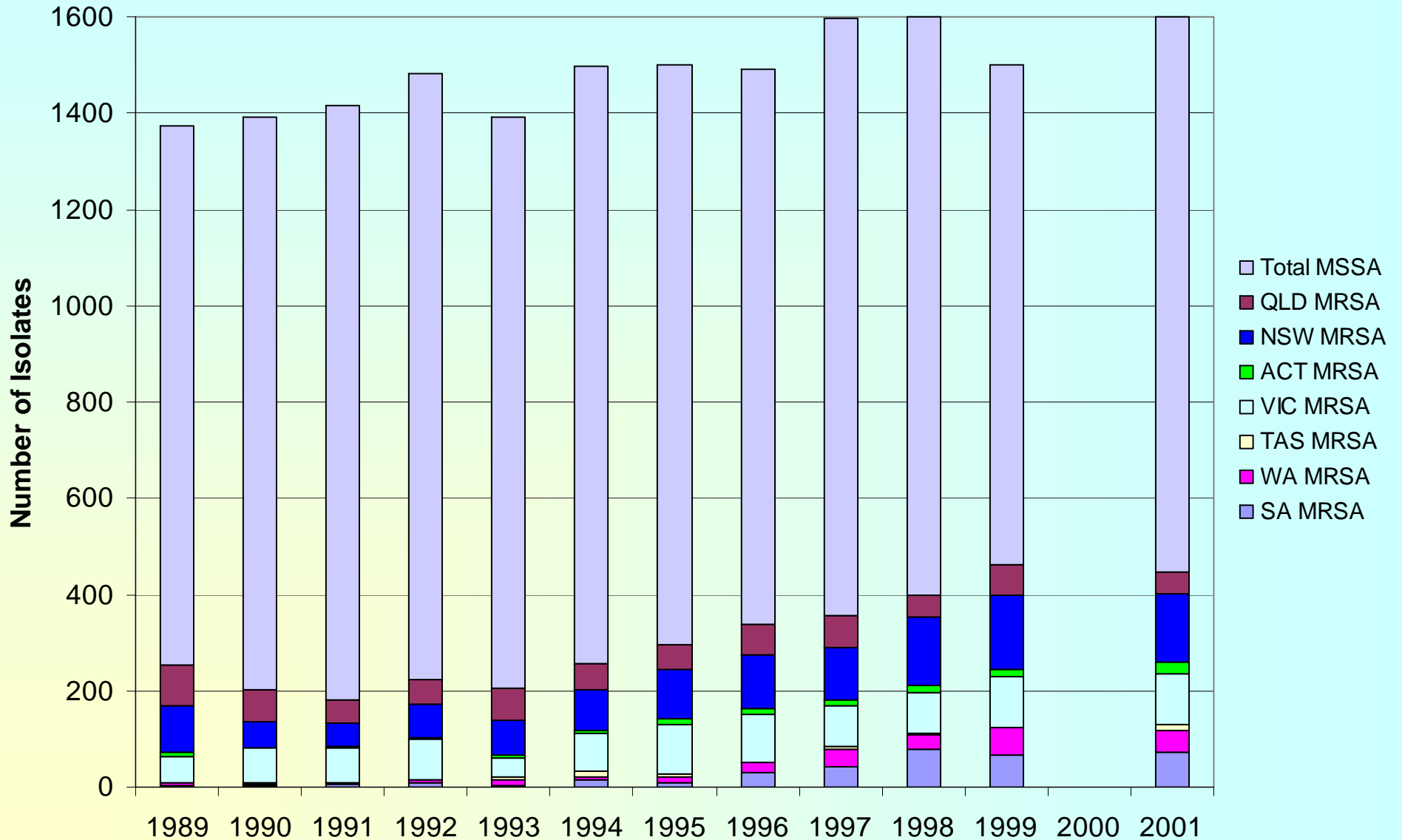
AGAR Staphylococcus aureus Survey

- Susceptibility results (1989-99, 2001)
- Typing results (2001)

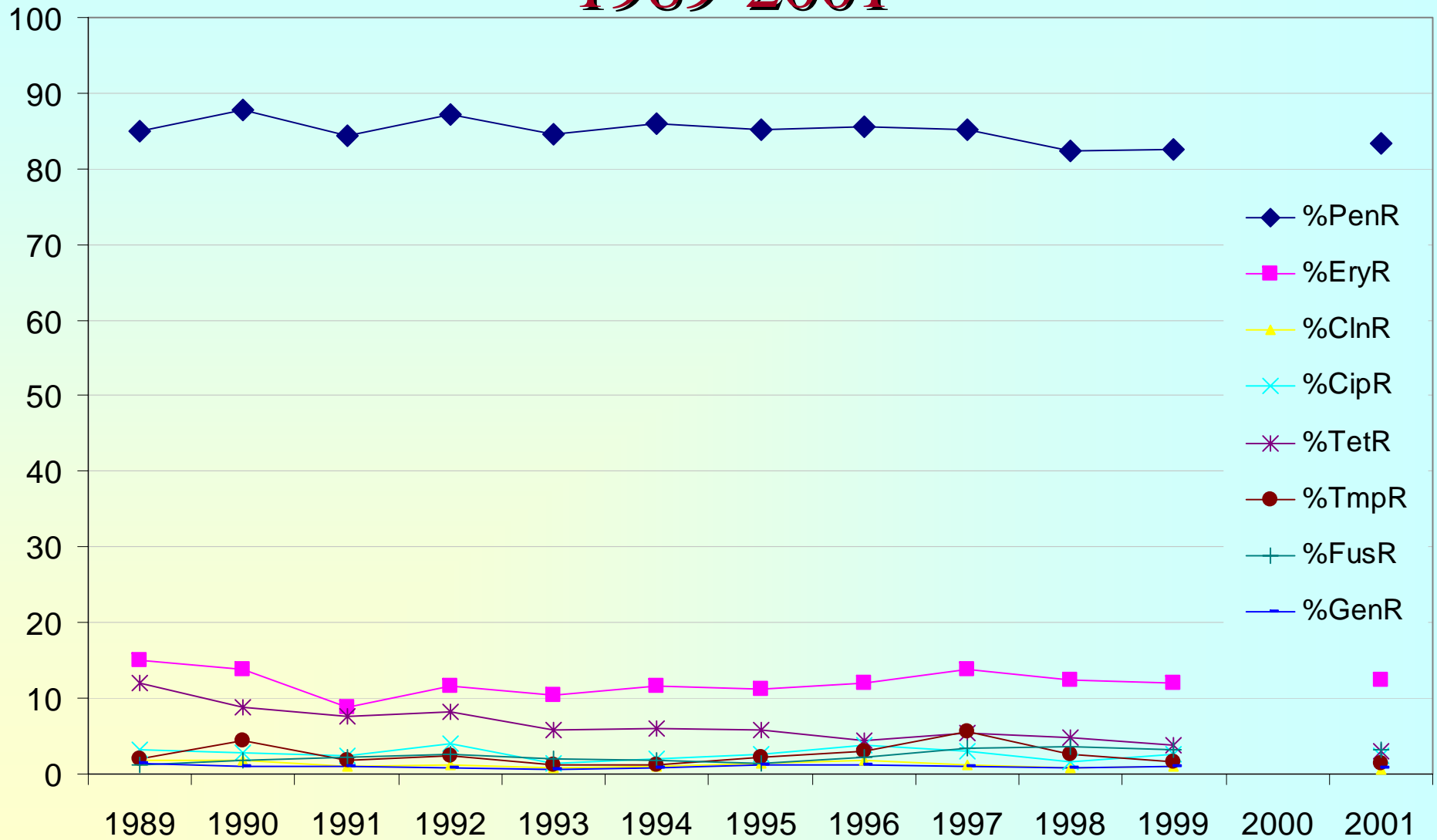
AGAR *S. aureus* Hospital Survey 1989-2001



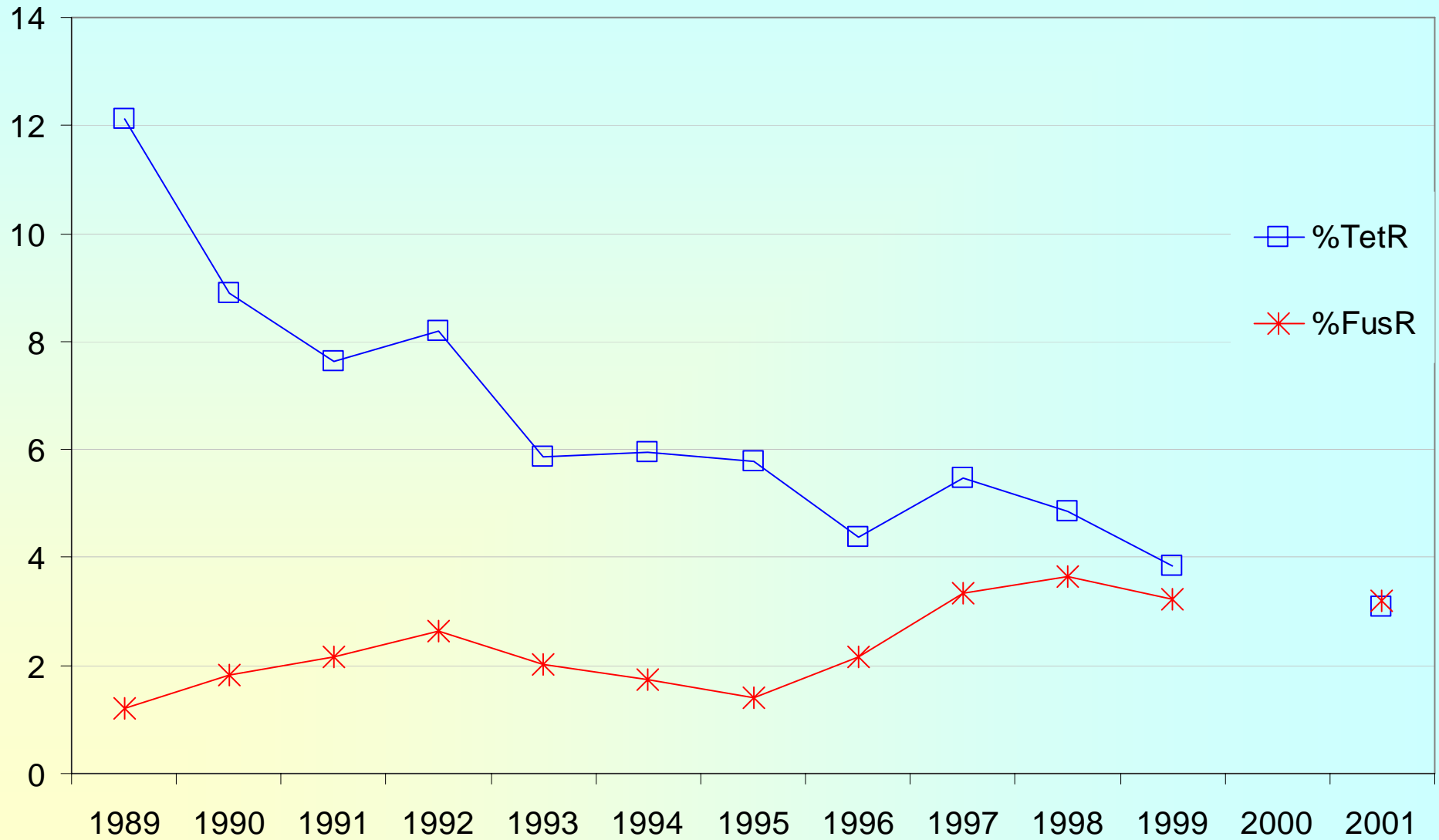
Susceptibility of *S. aureus* to Methicillin 1989-2001



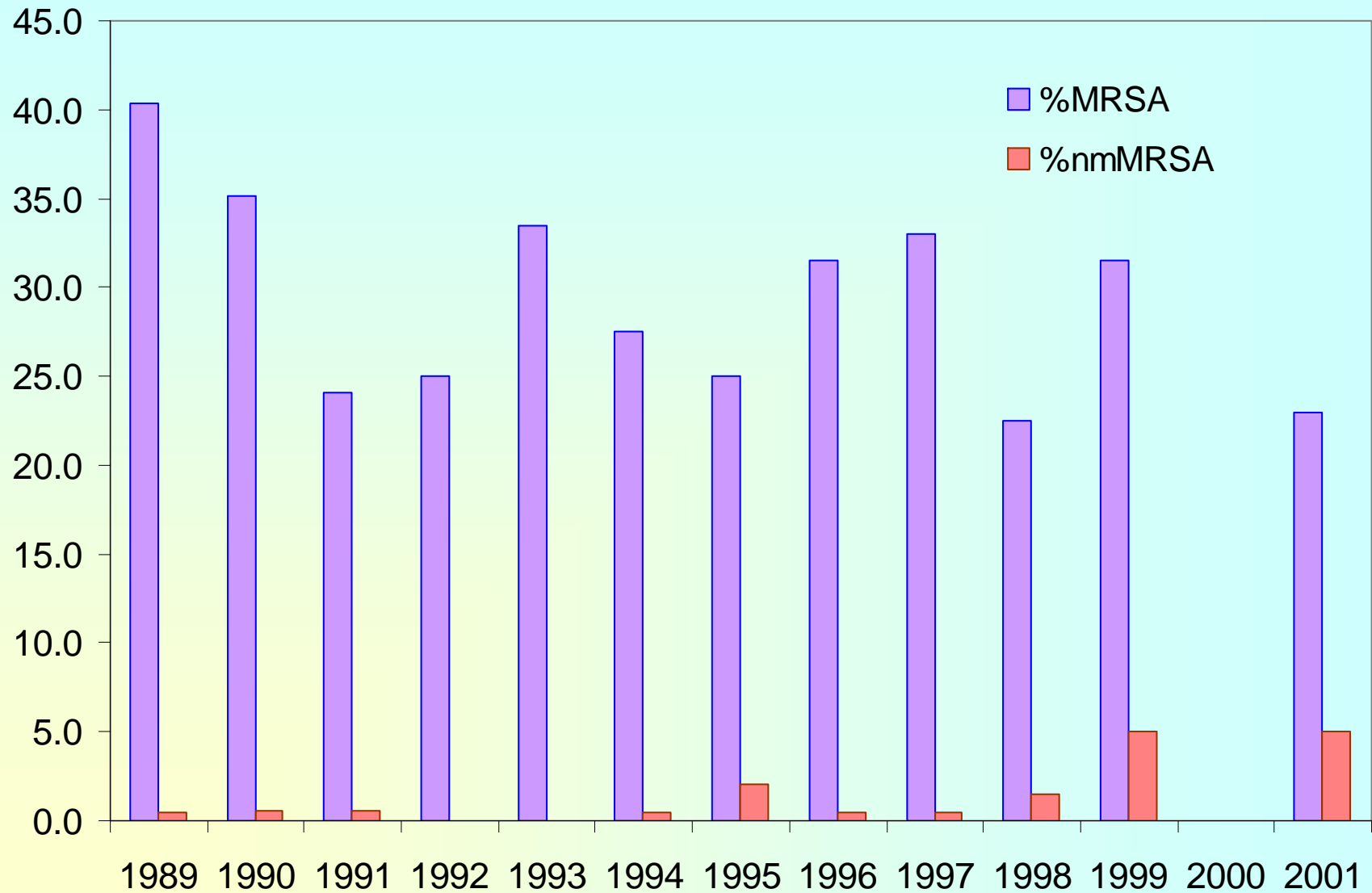
Trends in Resistance in MSSA 1989-2001



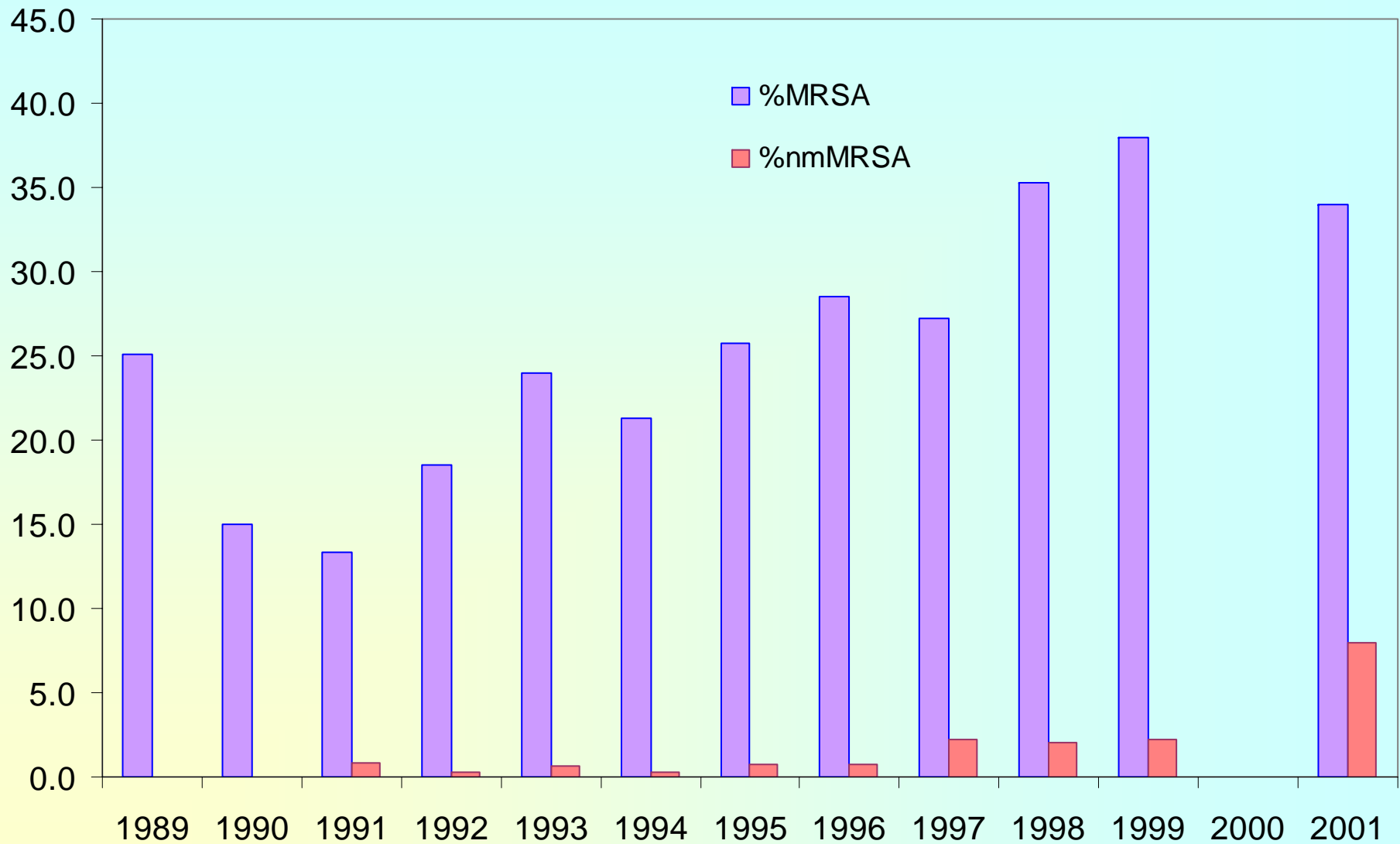
Trends in Resistance in MSSA 1989-2001



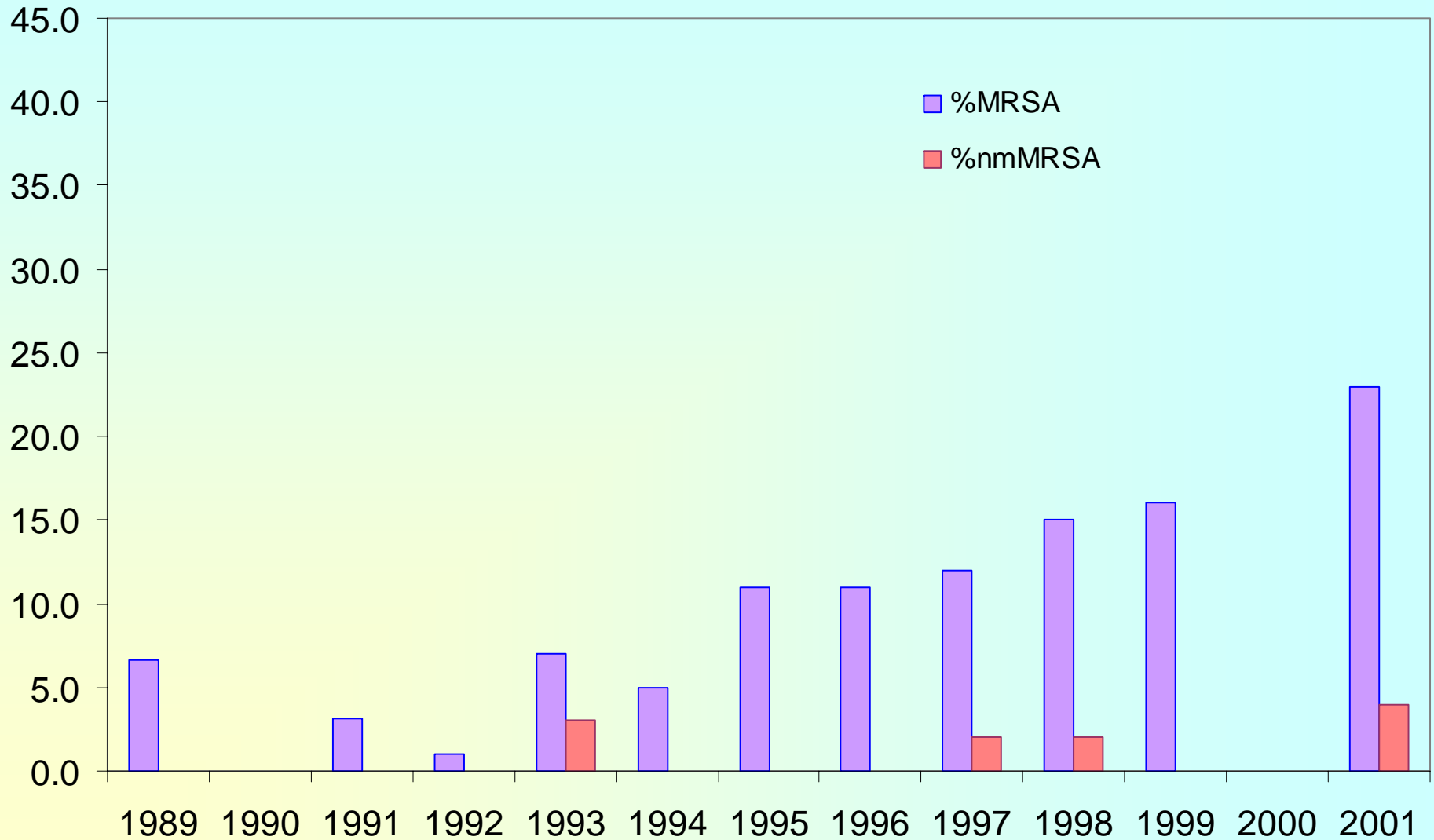
MRSA in Brisbane 1989-2001



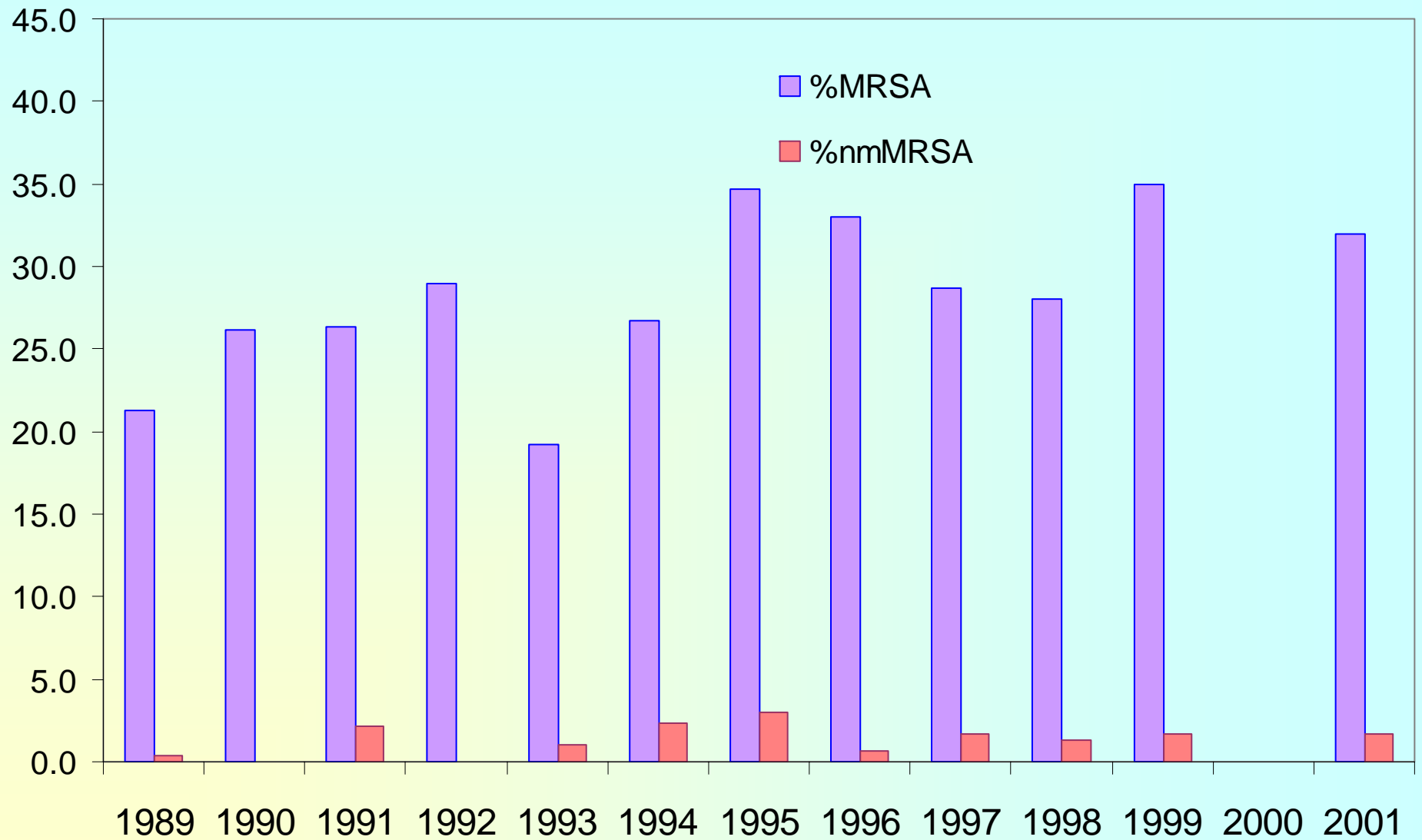
MRSA in Sydney 1989-2001



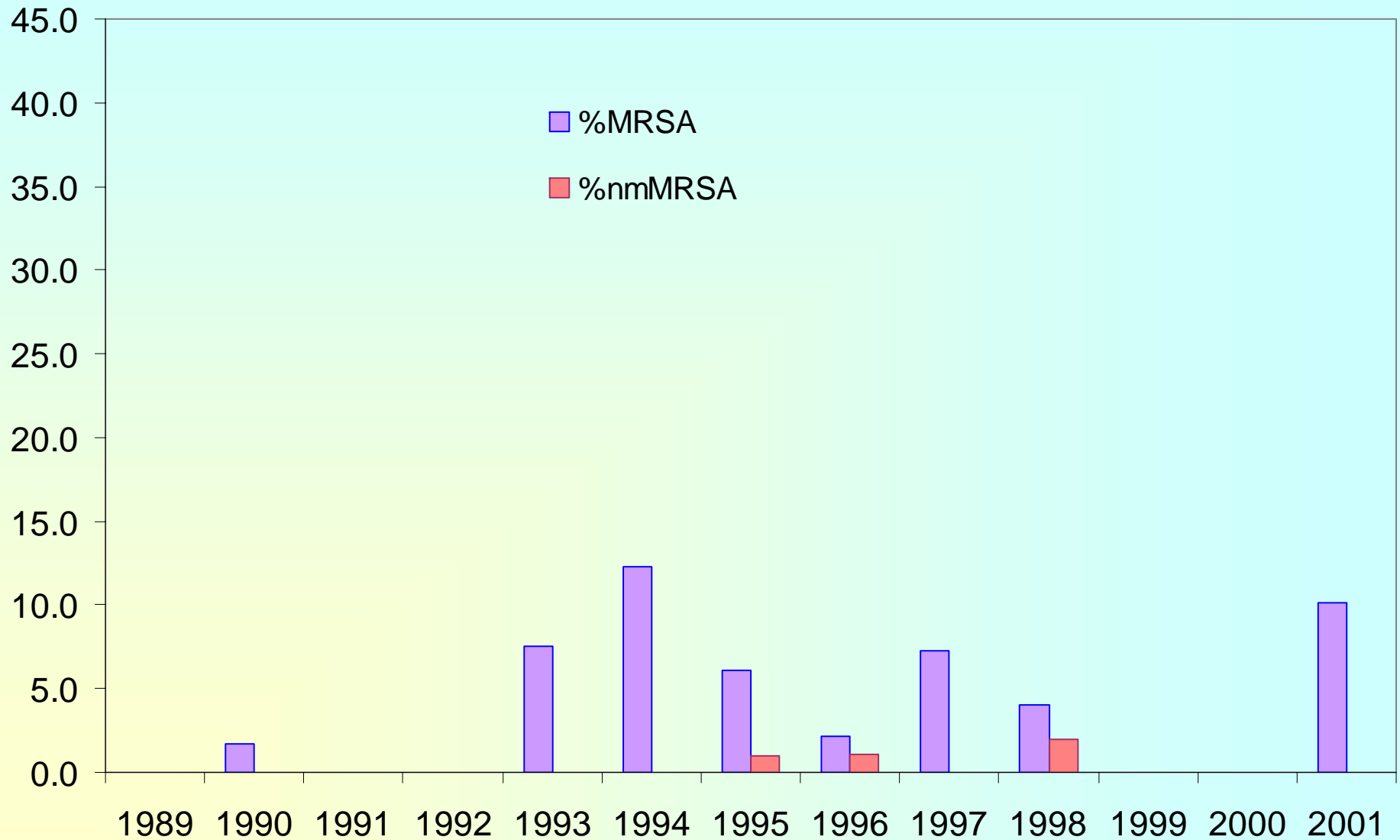
MRSA in Canberra 1989-2001



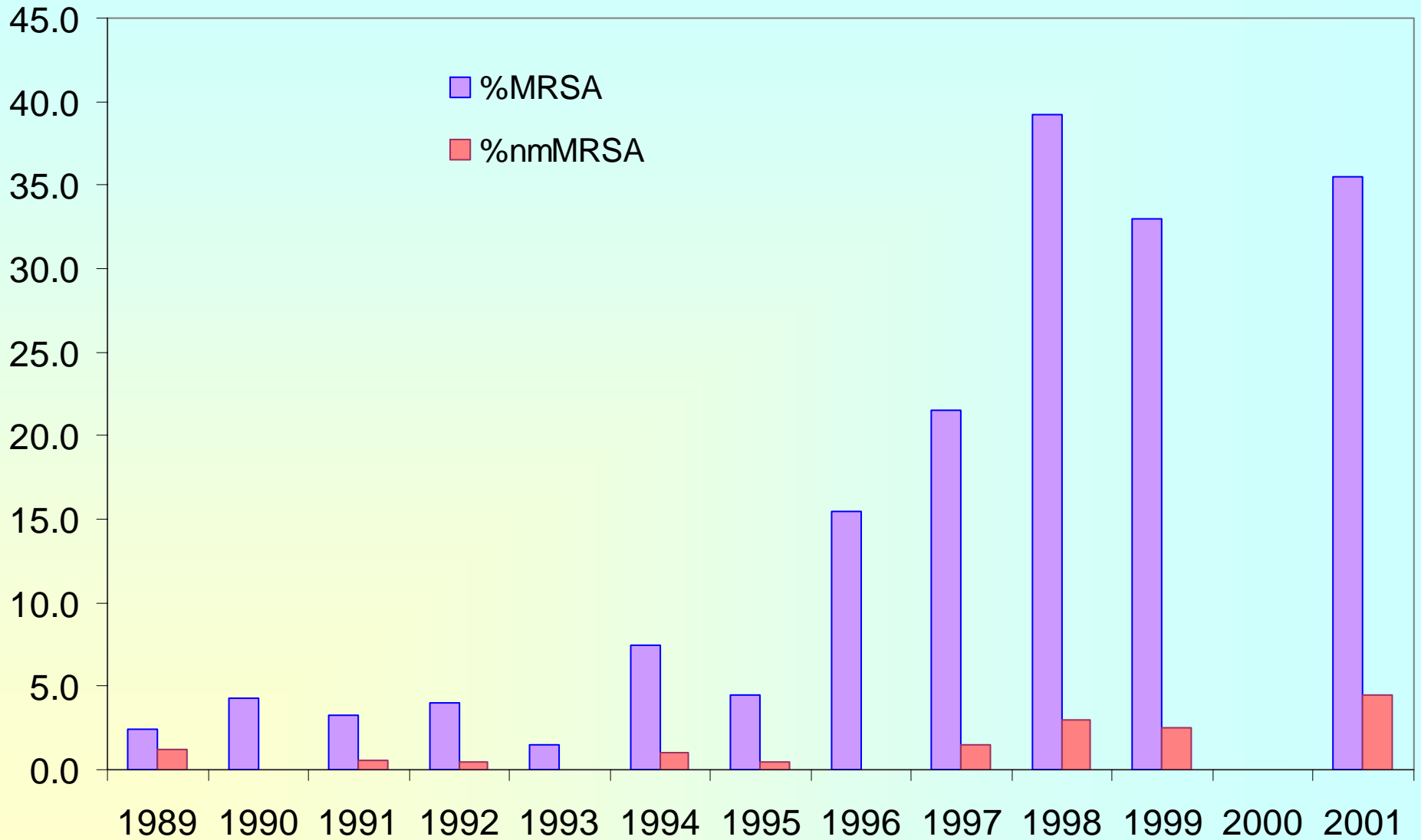
MRSA in Melbourne 1989-2001



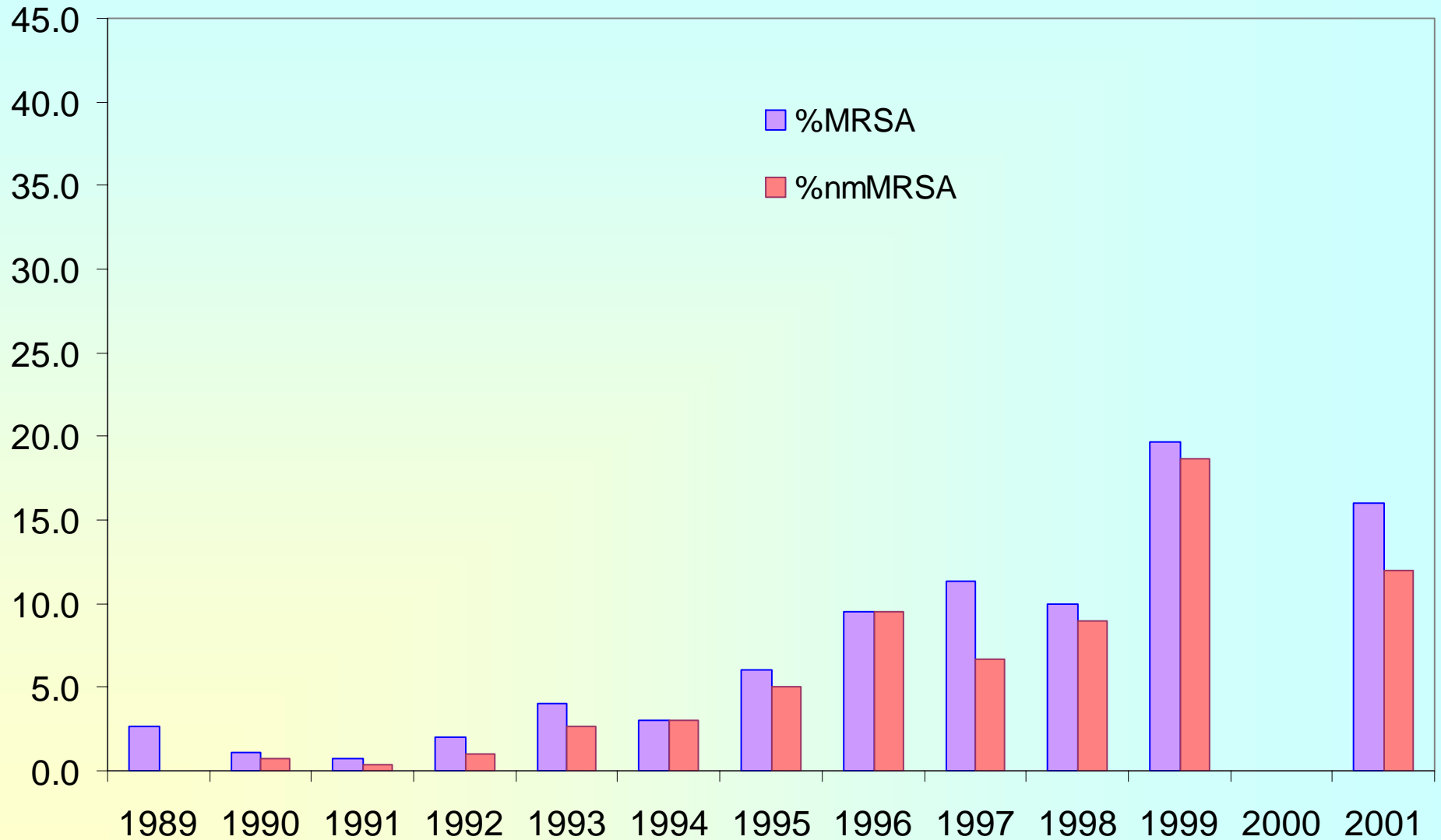
MRSA in Hobart 1989-2001



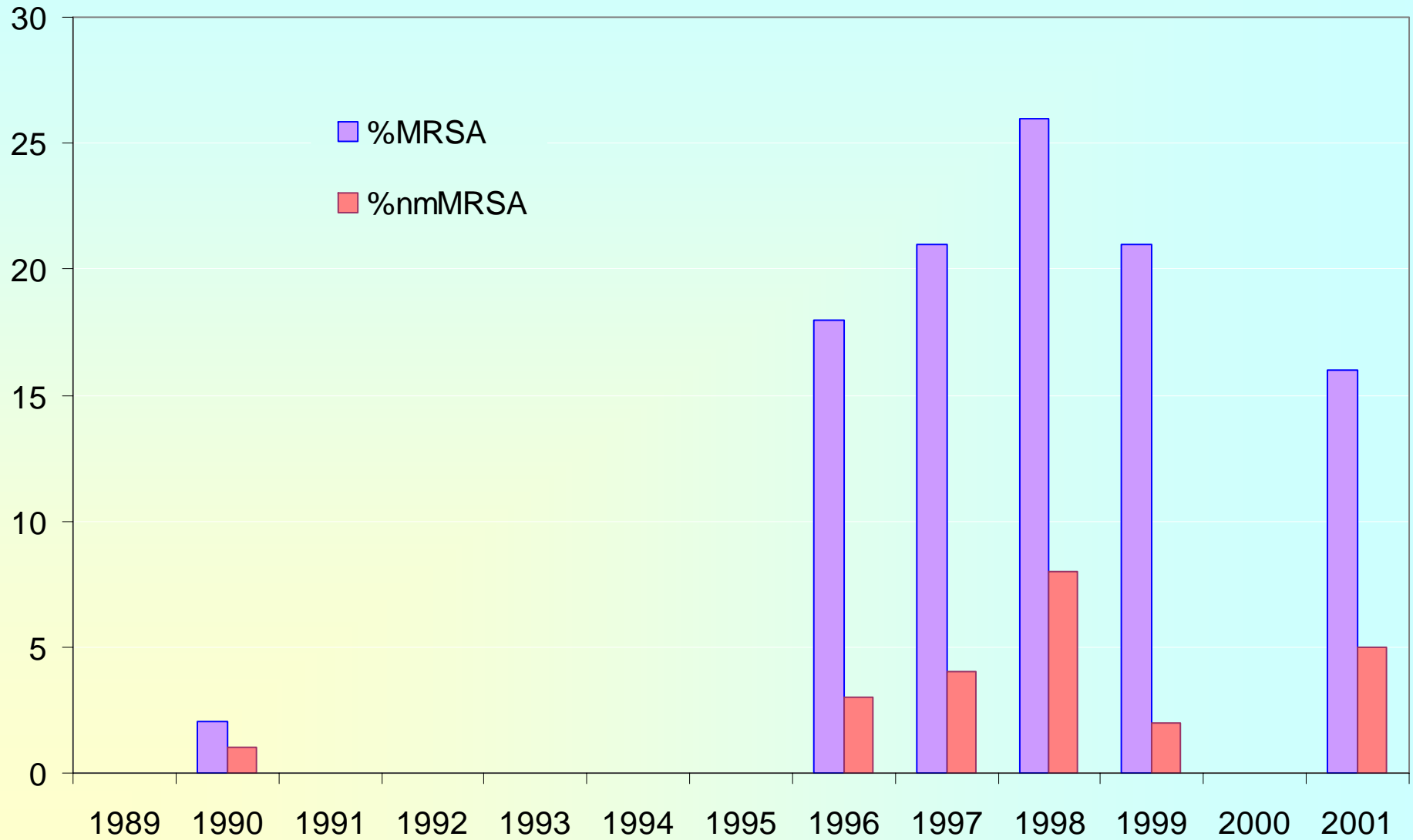
MRSA in Adelaide 1989-99



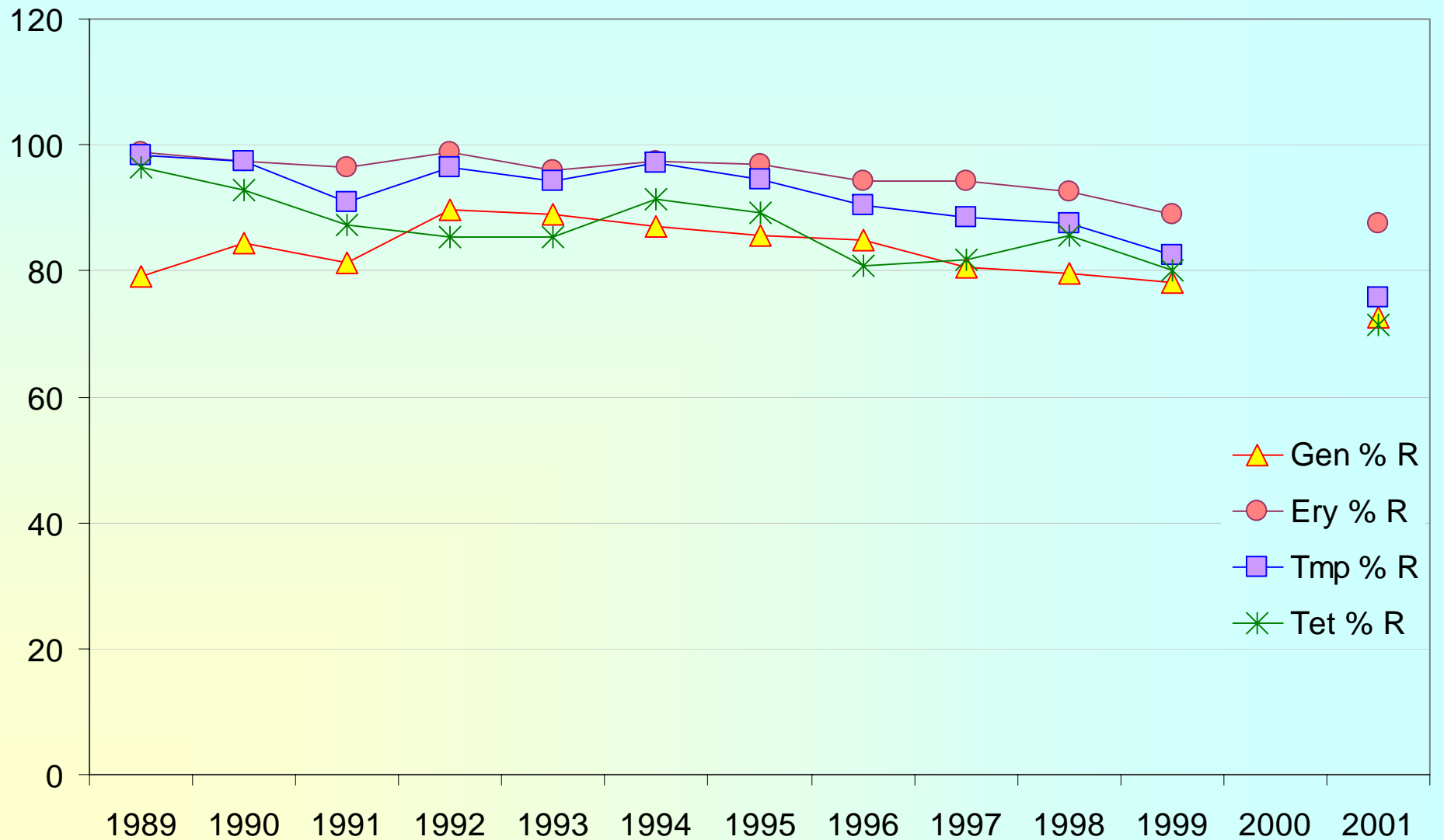
MRSA in Perth 1989-2001



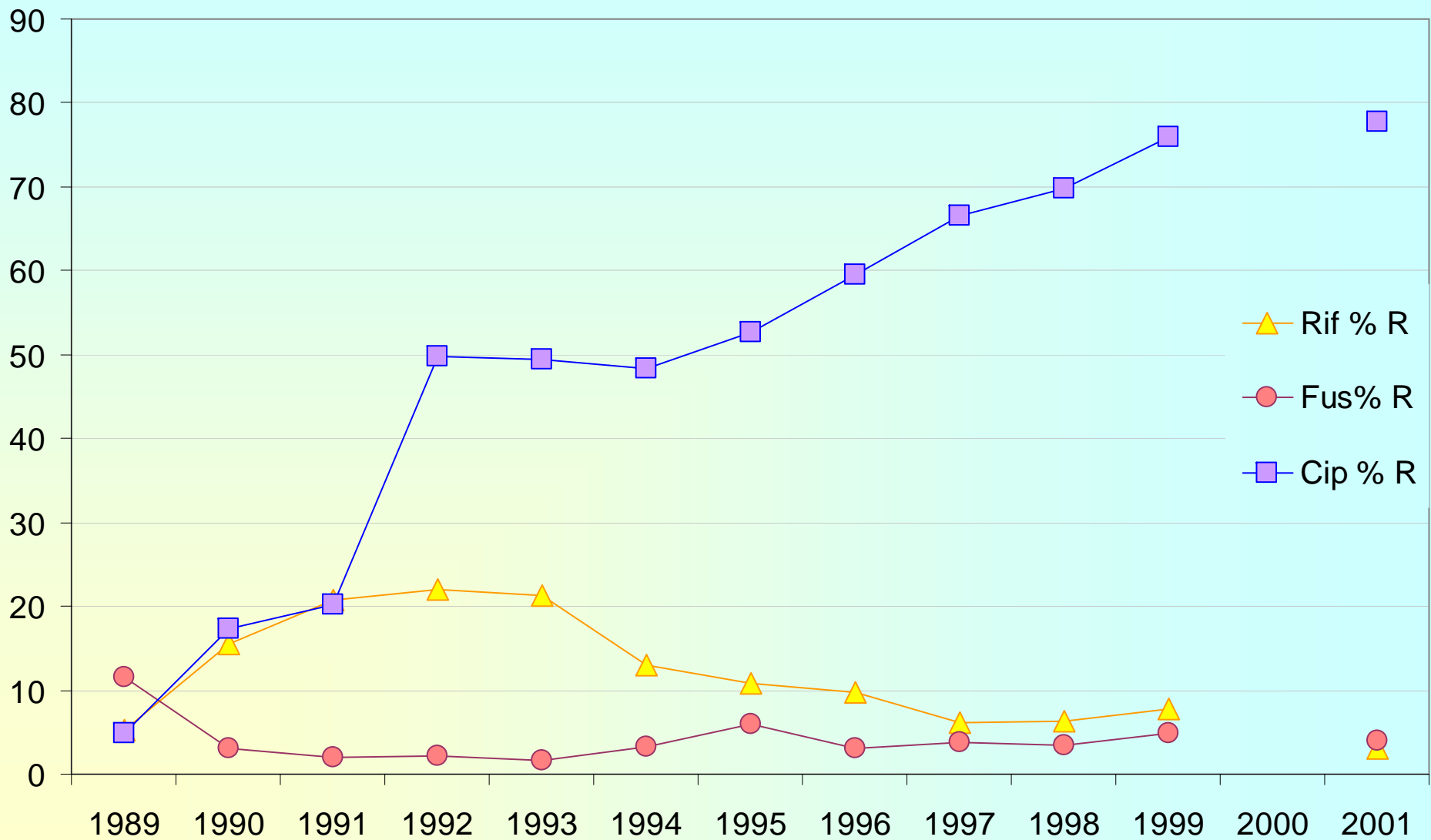
MRSA in Darwin 1990-99



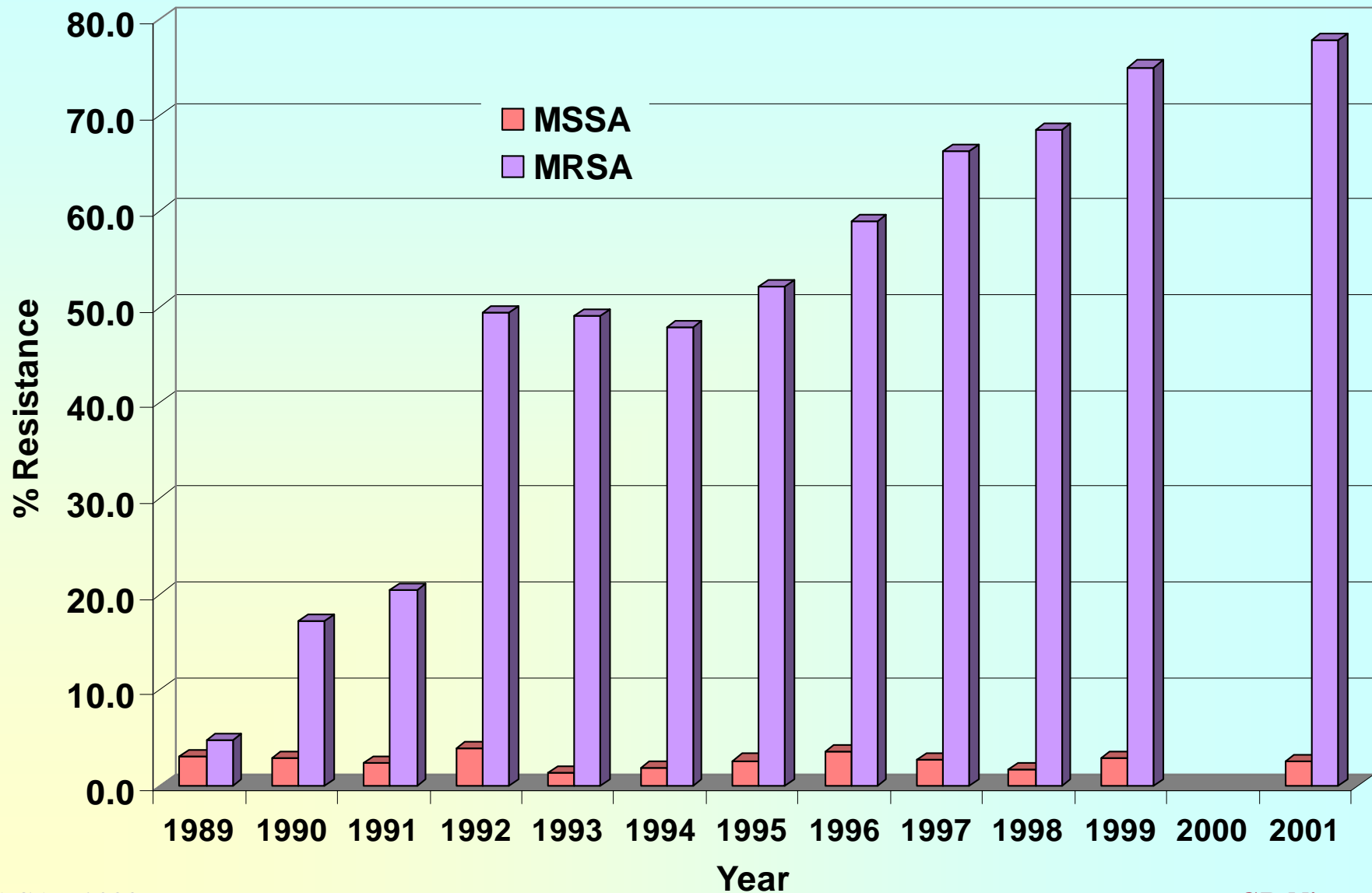
Trends in Resistance in MRSA 1989-2001



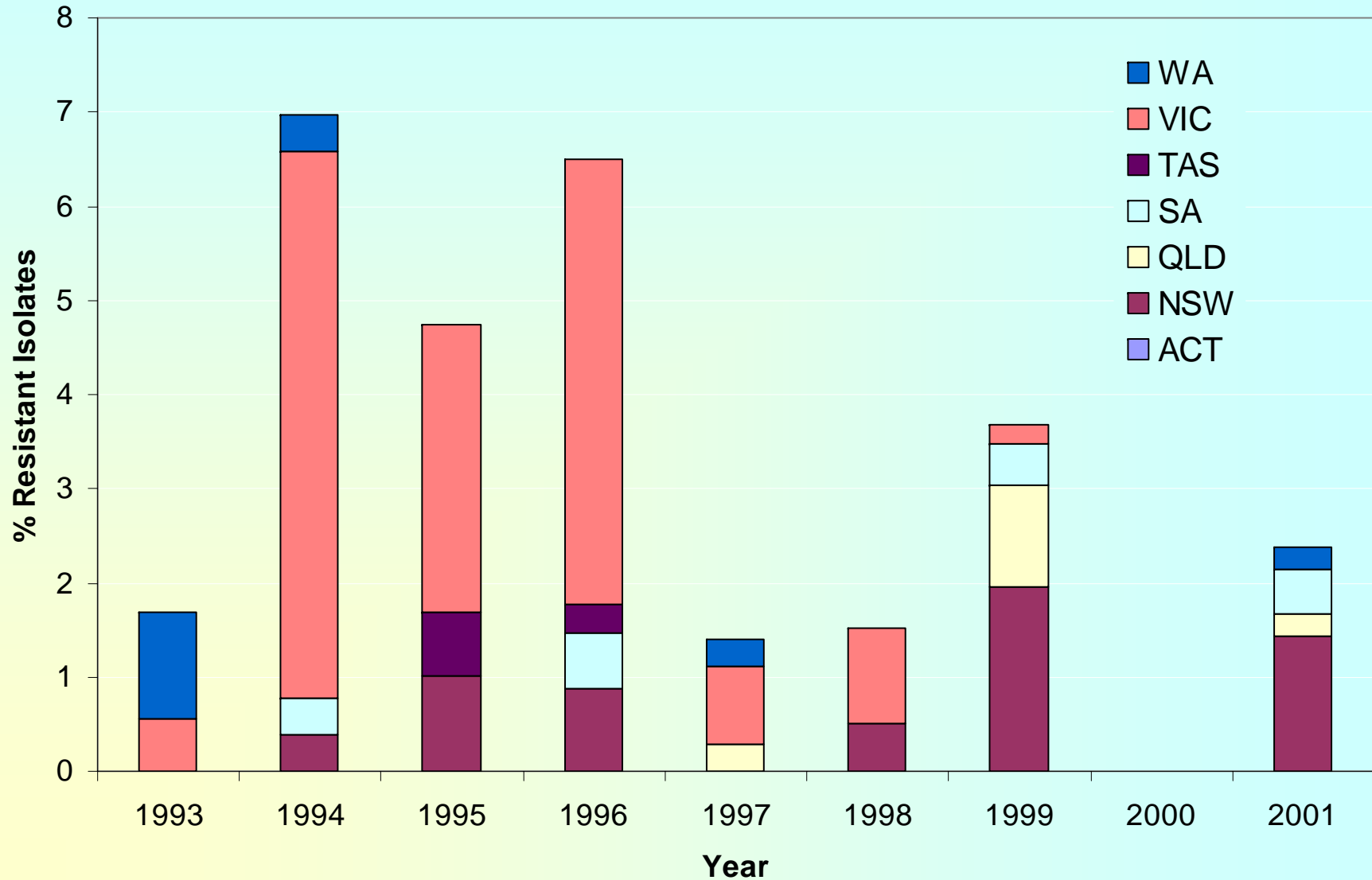
Trends in Resistance in MRSA 1989-2001



Ciprofloxacin resistance in MRSA



Mupirocin Resistance in MRSA 1993-2001



MRSA Typing

- Antibiogram/resistogram
- Phage typing
- Plasmid profiles
- Zymotyping
- PFGE
- Coagulase PCR RFLP
- *spa* typing
- **Multilocus sequence typing (MLST)**
- ***mec* gene complex (SCC *mec*) typing**

MLST

- Alleles in 7 unlinked house keeping genes (core genome) by sequencing
- Allelic profiles: $n-n-n-n-n-n-n$
- Sequence type: $ST\ N$

Enright et al J Clin Microbiol 2000; 38:1008-15

Multiresistant MRSA in Australia 2001

	Usually Resistant to	Urease	Phage susceptibility (typical)	Coagulase PCR/RFLP	MLST*
AUS-2	Tet, Ery, Tmp, Gen, Cip	+	85/88/90//47T/87M//MR8/MR12/M3	24	239
AUS-3	Tet, Ery, Tmp, Gen, Cip, HgCl ₂ , phenyl Hg acetate	+	87M/M3	24	239
Irish 2	Ery, Tmp, Cip	-	85/90//90A/87M		8
Sporadic	Variable	+	Variable		?

*Based on 2000 survey results

- All readily distinguished by PFGE

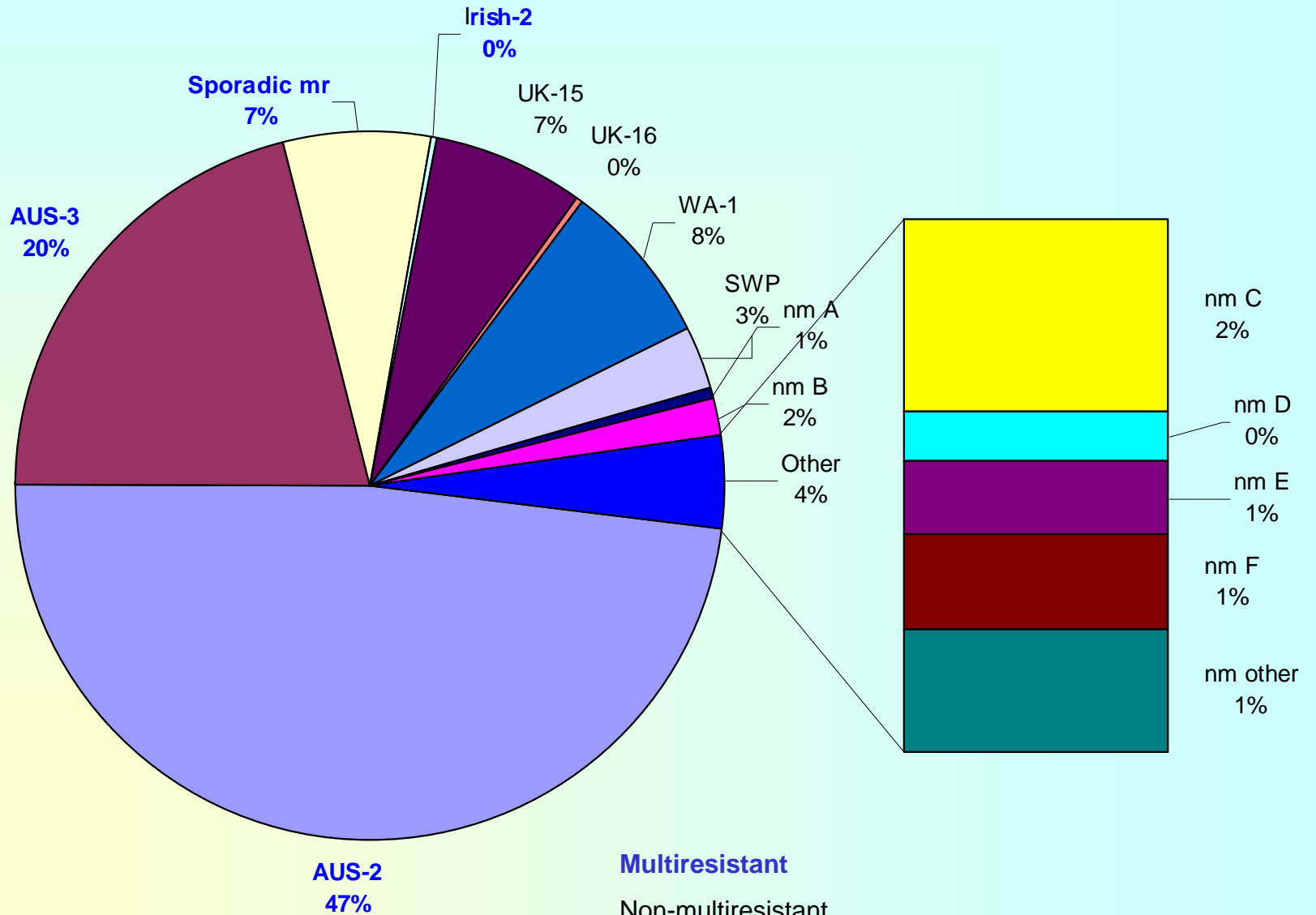
Non-multiresistant MRSA in Australia 2001

	Usually Resistant to	Urease	Phage susceptibility (typical)	Coagulase PCR/RFLP	MLST*
UK EMRSA-15	Ery, Cip	-	Non-typable	22	22
SWP	NI	+	WSPP1 – 29/52/52A/80/3A/5A/77/81 WSPP2 – 6/42E/47/54/77/81//67R	24	30
WA MRSA 1	Ery	+	1A – non-typable 1B – 52A/55/6/42E/47/53/54/77/83A/85/88/90	20	1
Other 'pulsotypes'	Variable	+	Variable	Variable	Variable

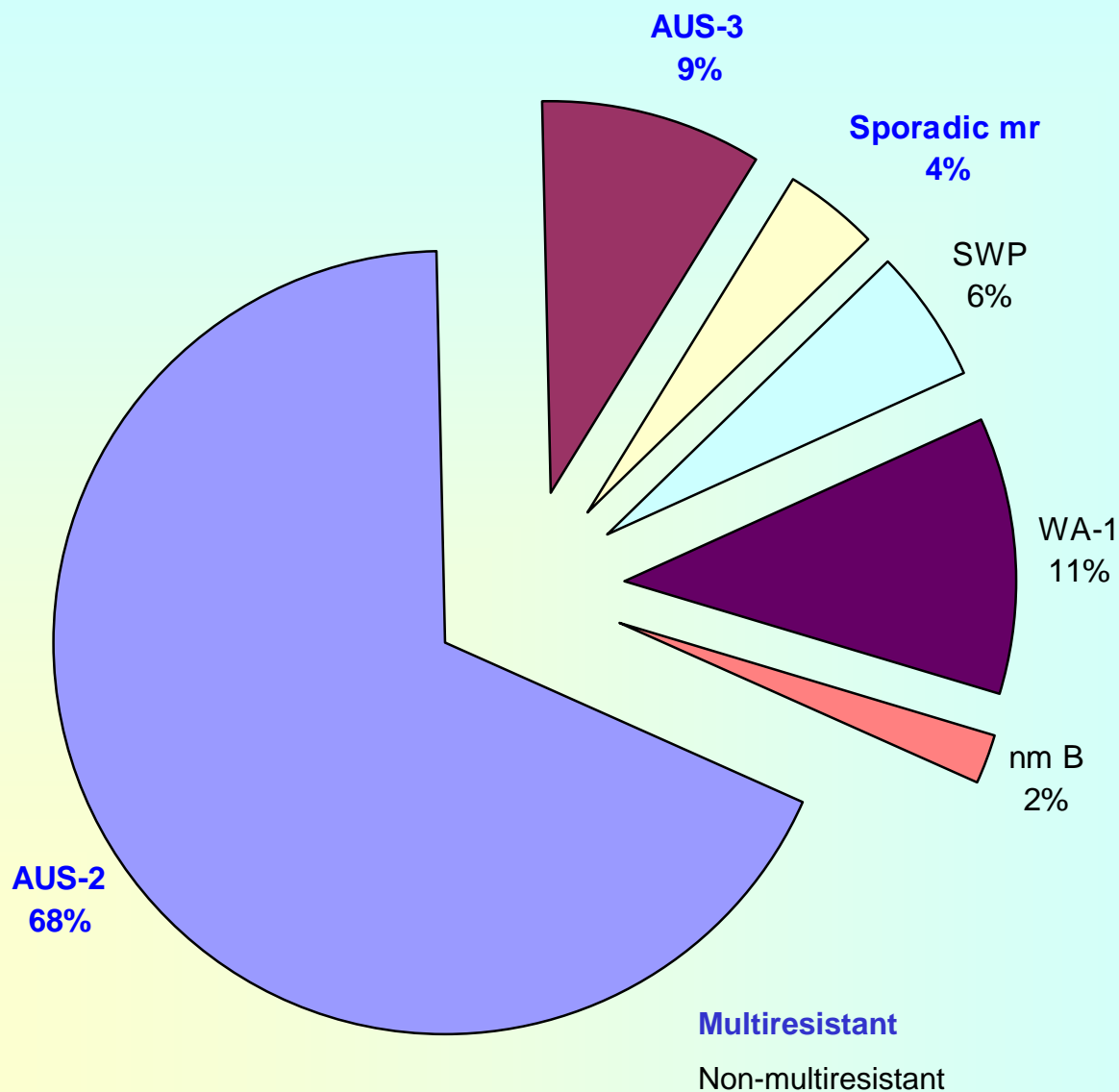
*Based on 2000 survey results

- All readily distinguished by PFGE

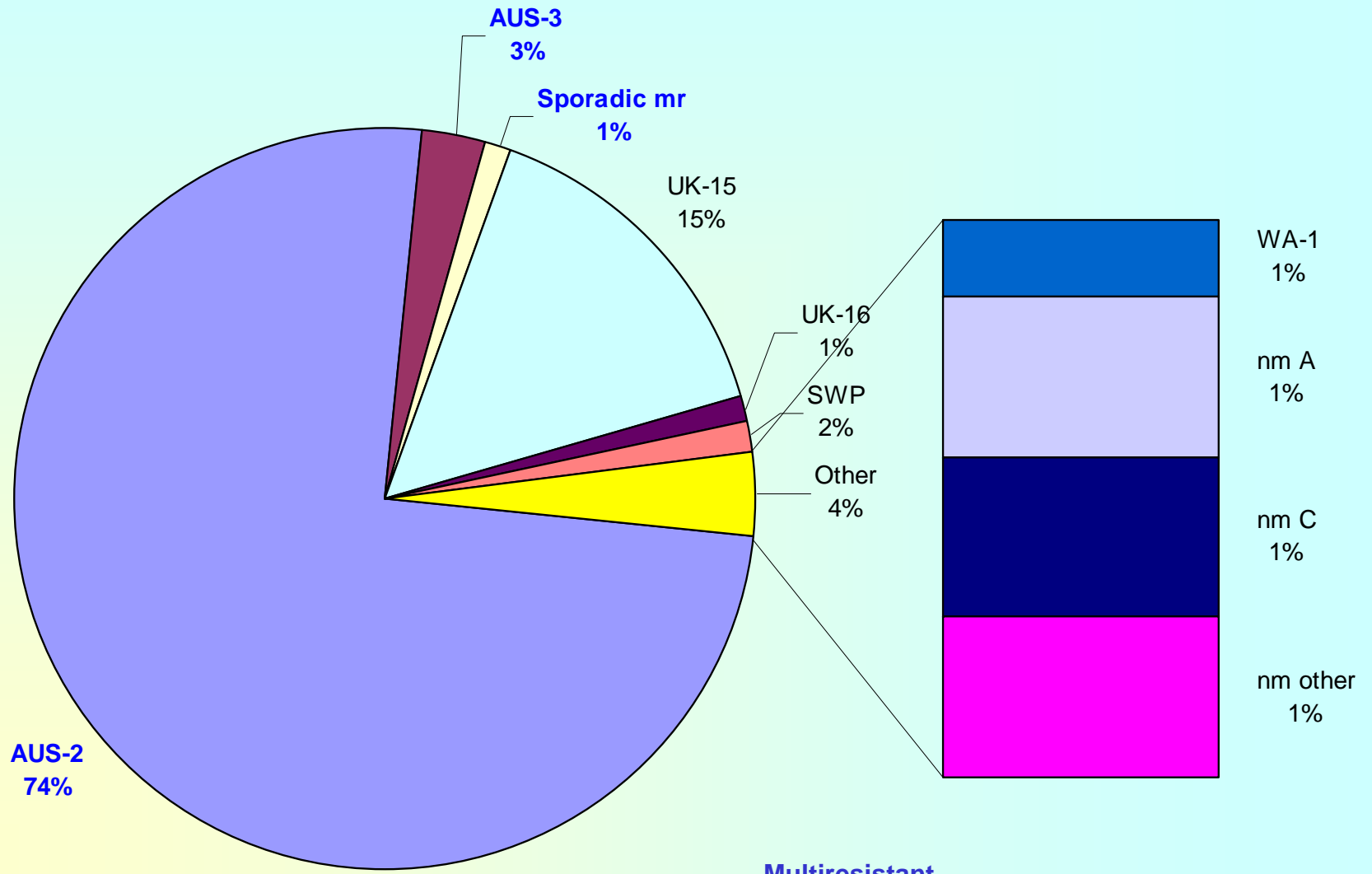
National MRSA Typing Results 2001 - 530 Isolates



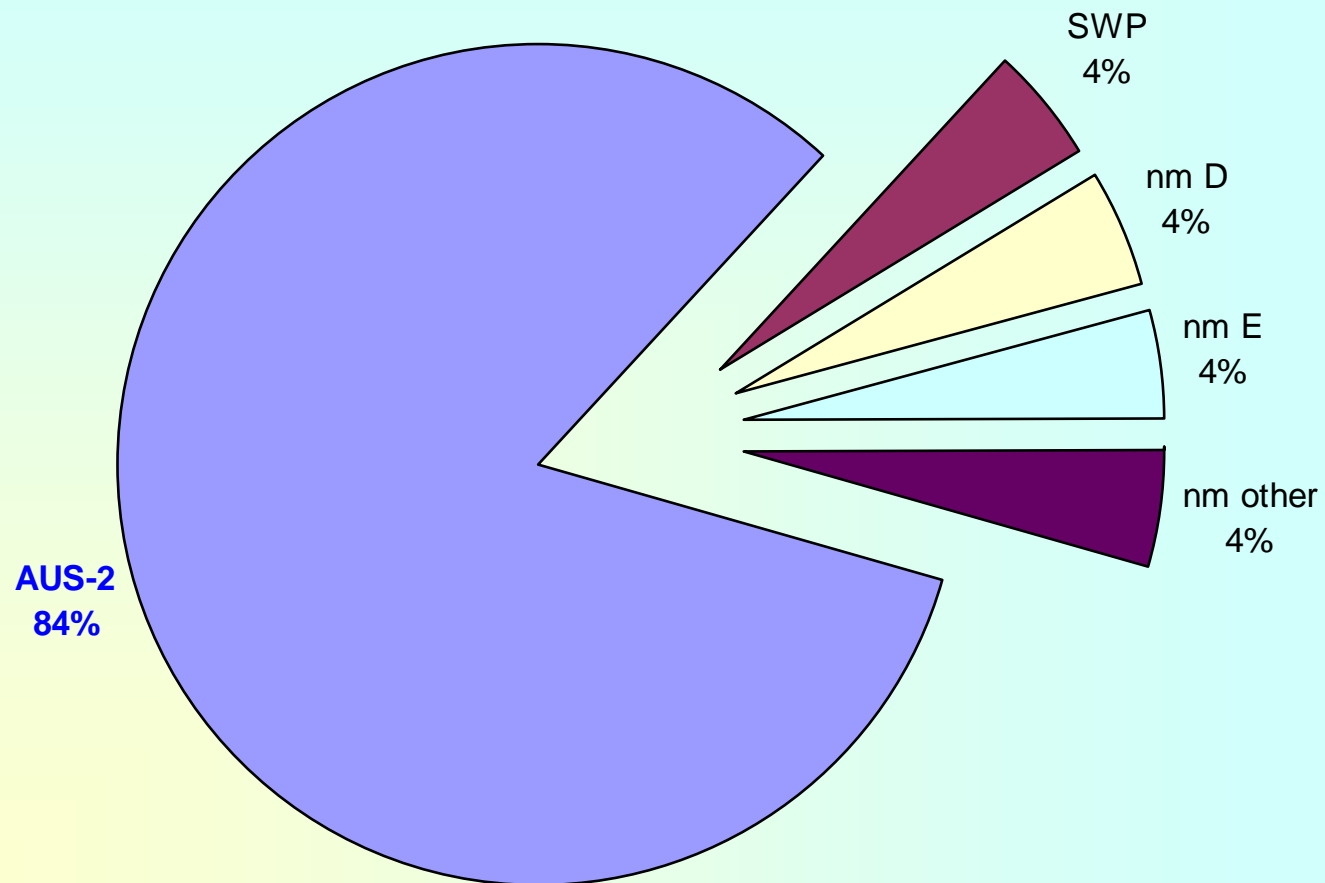
Queensland MRSA Typing Results 2001 - 53 Isolates



New South Wales MRSA Typing Results 2001 - 199 Isolates



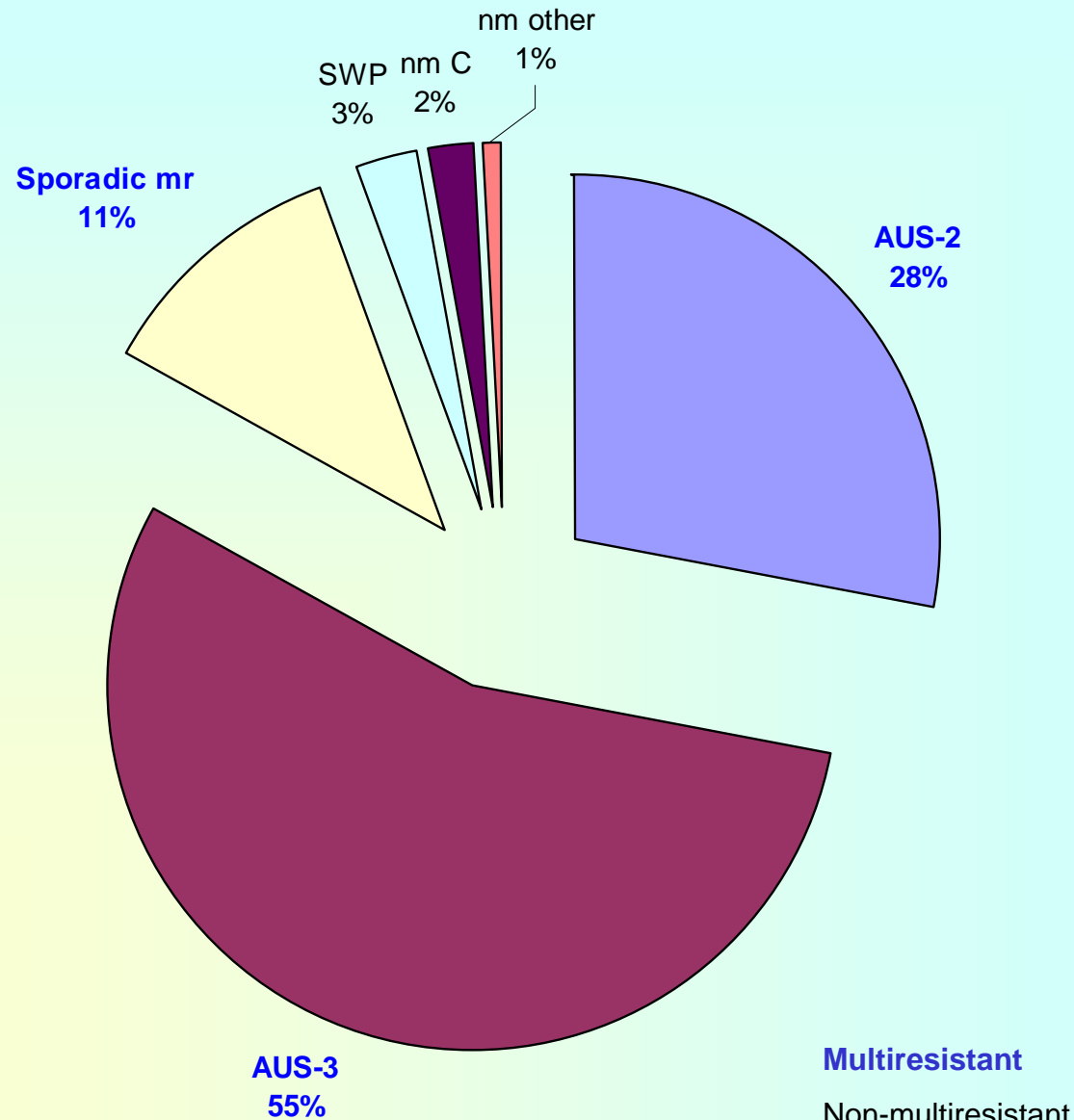
ACT MRSA Typing Results 2001 - 23 Isolates



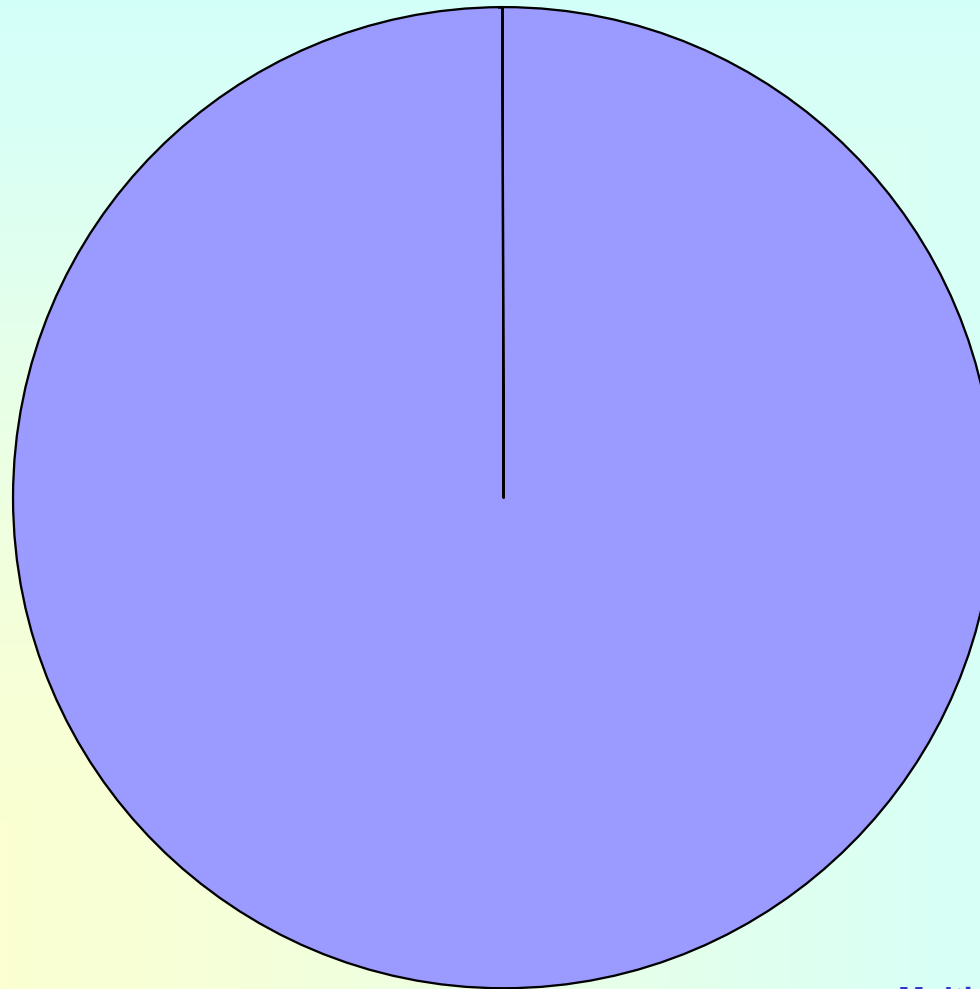
Multiresistant

Non-multiresistant

Victoria MRSA Typing Results 2001 - 107 Isolates



Tasmania MRSA Typing Results 2001 - 10 Isolates

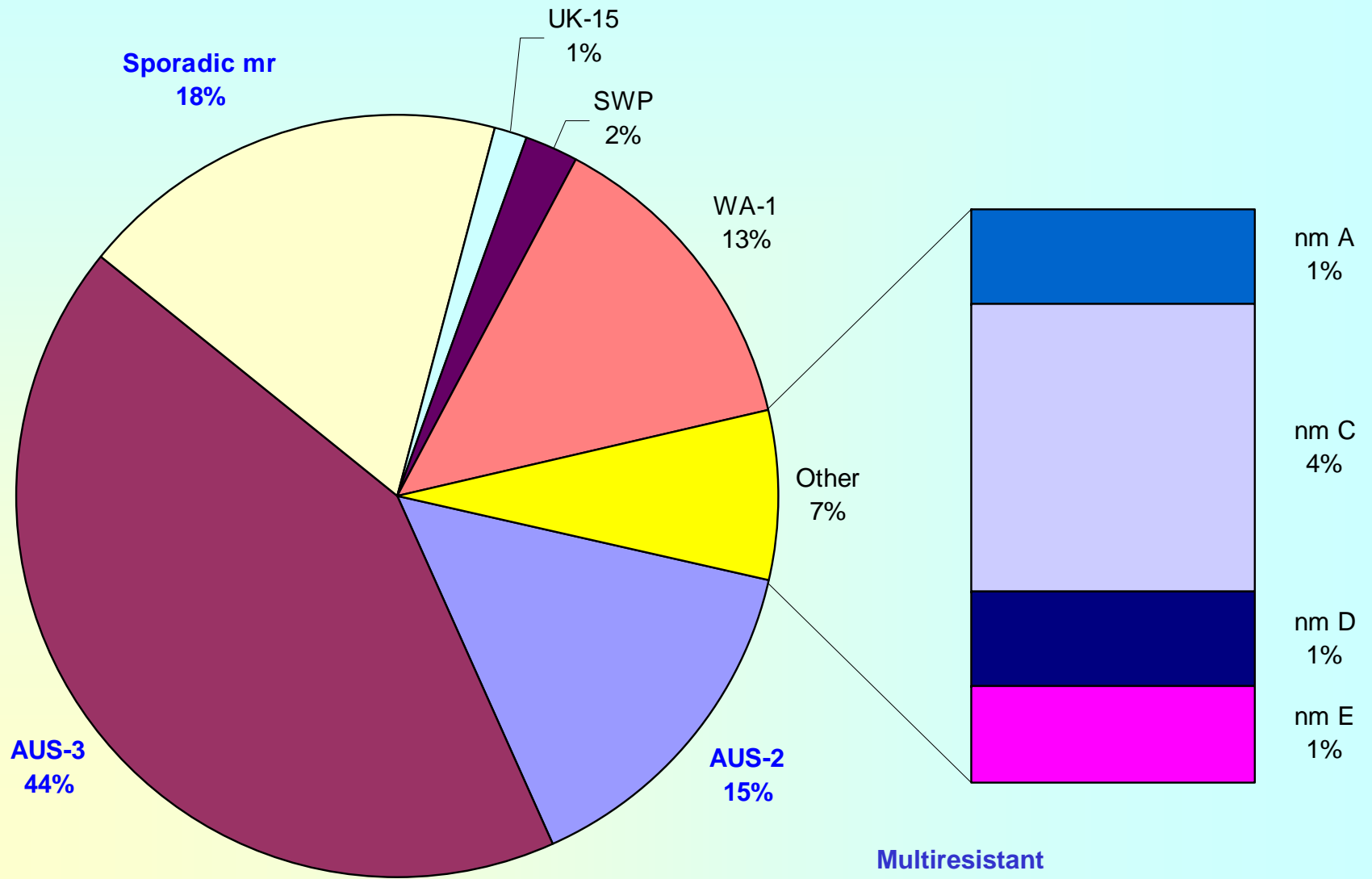


AUS-2 100%

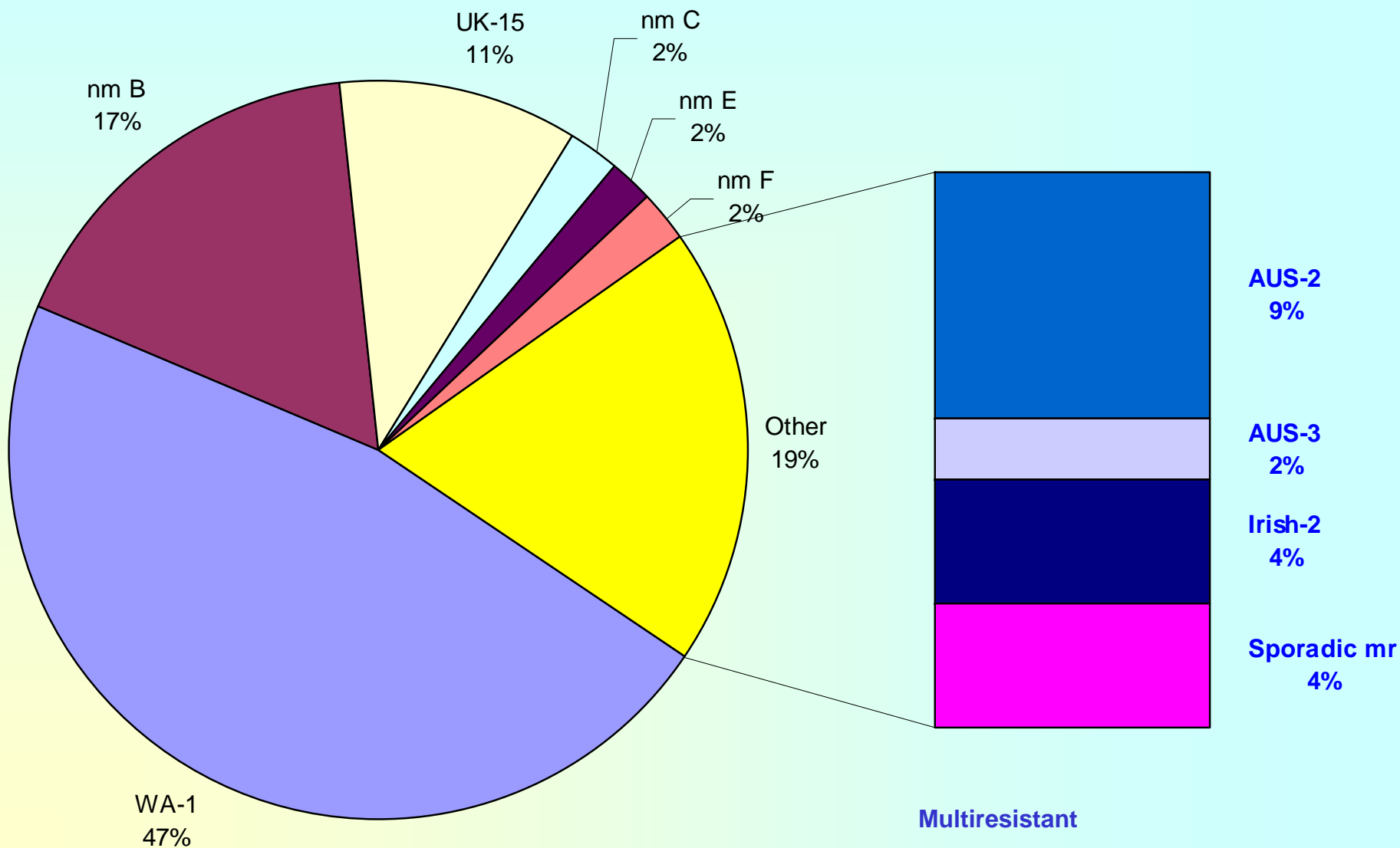
Multiresistant

Non-multiresistant

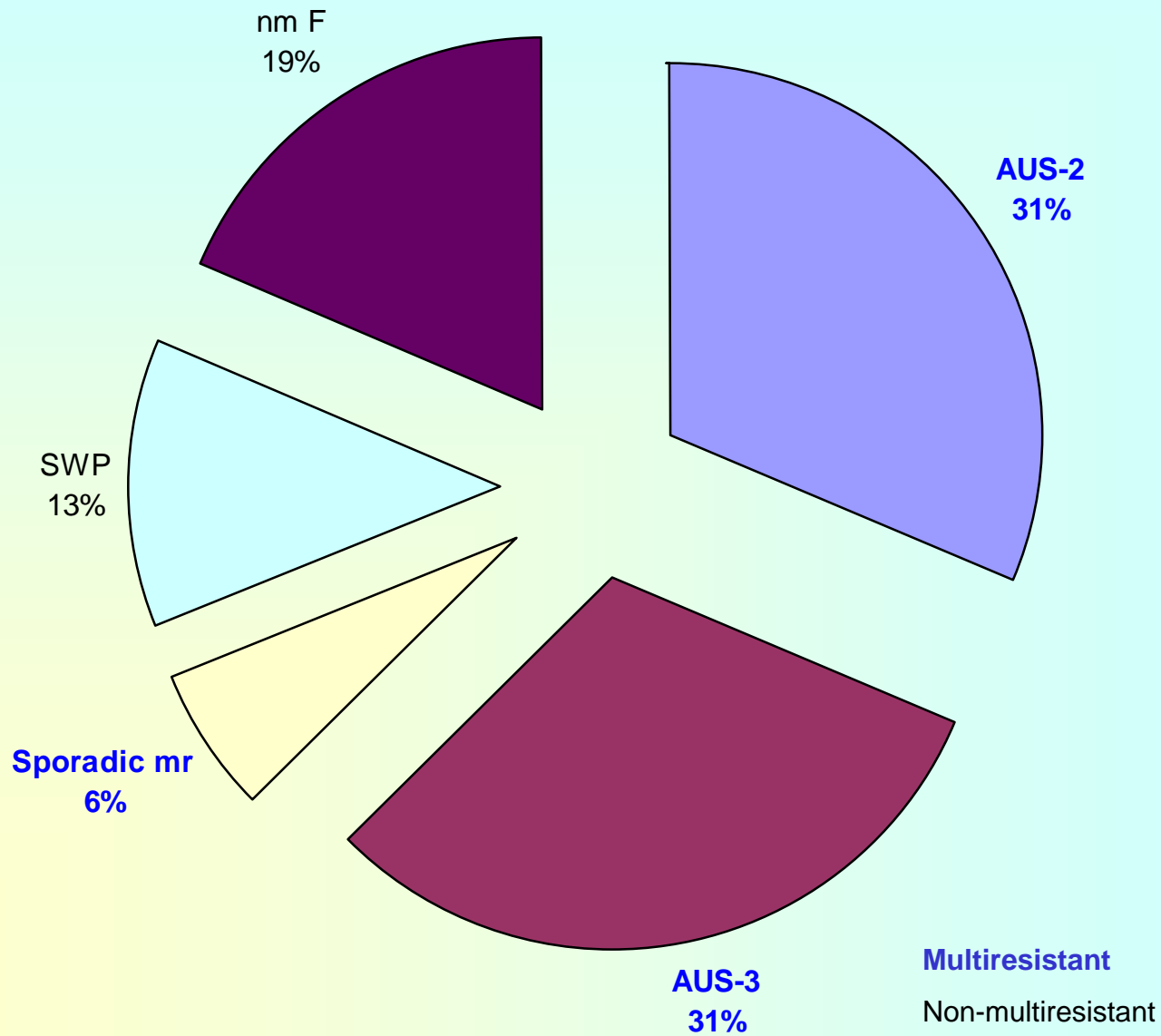
South Australia MRSA Typing Results 2001 - 82 Isolates



Western Australia MRSA Typing Results 2001 - 47 Isolates



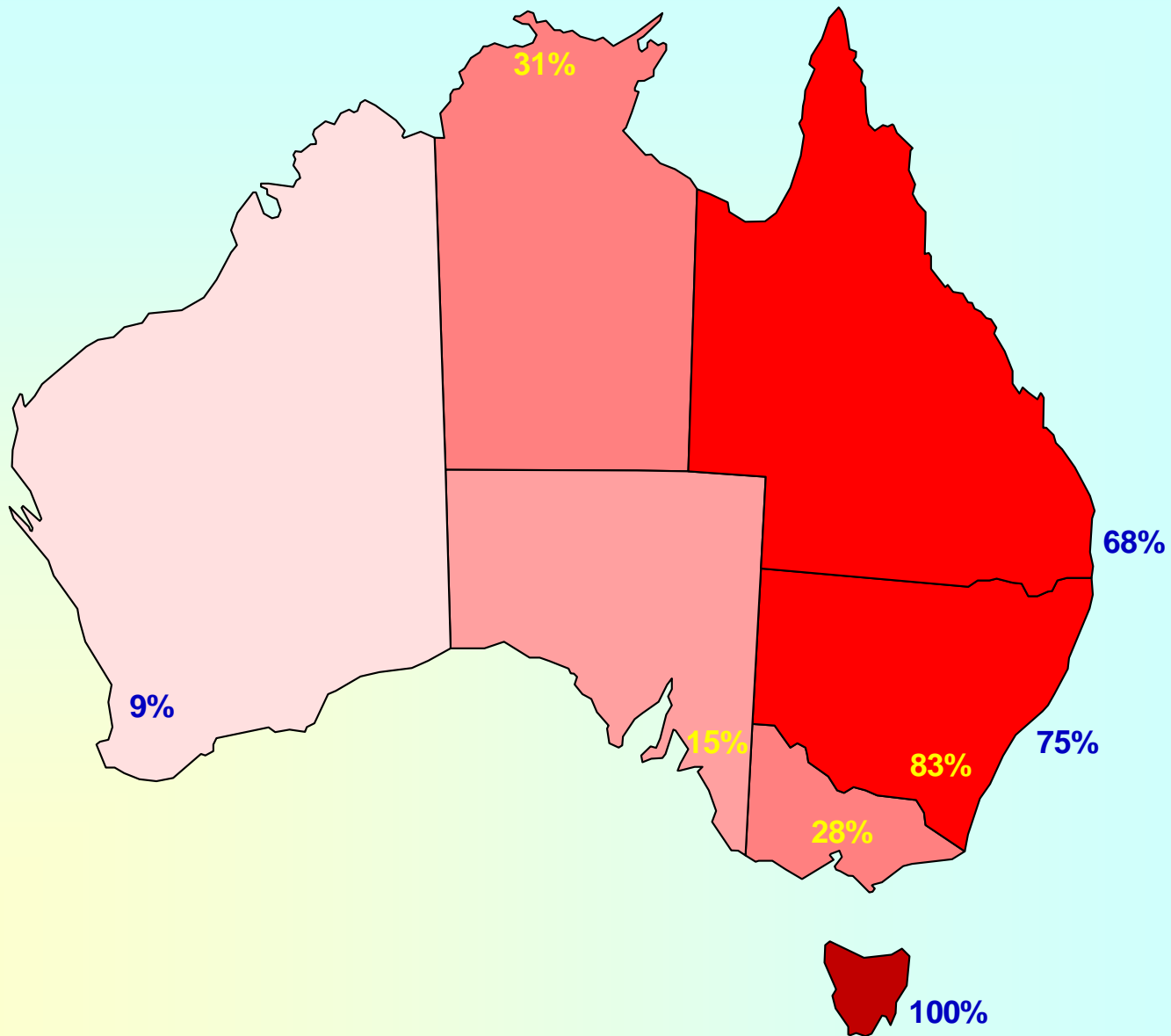
Northern Territory MRSA Typing Results 2001 - 16 Isolates



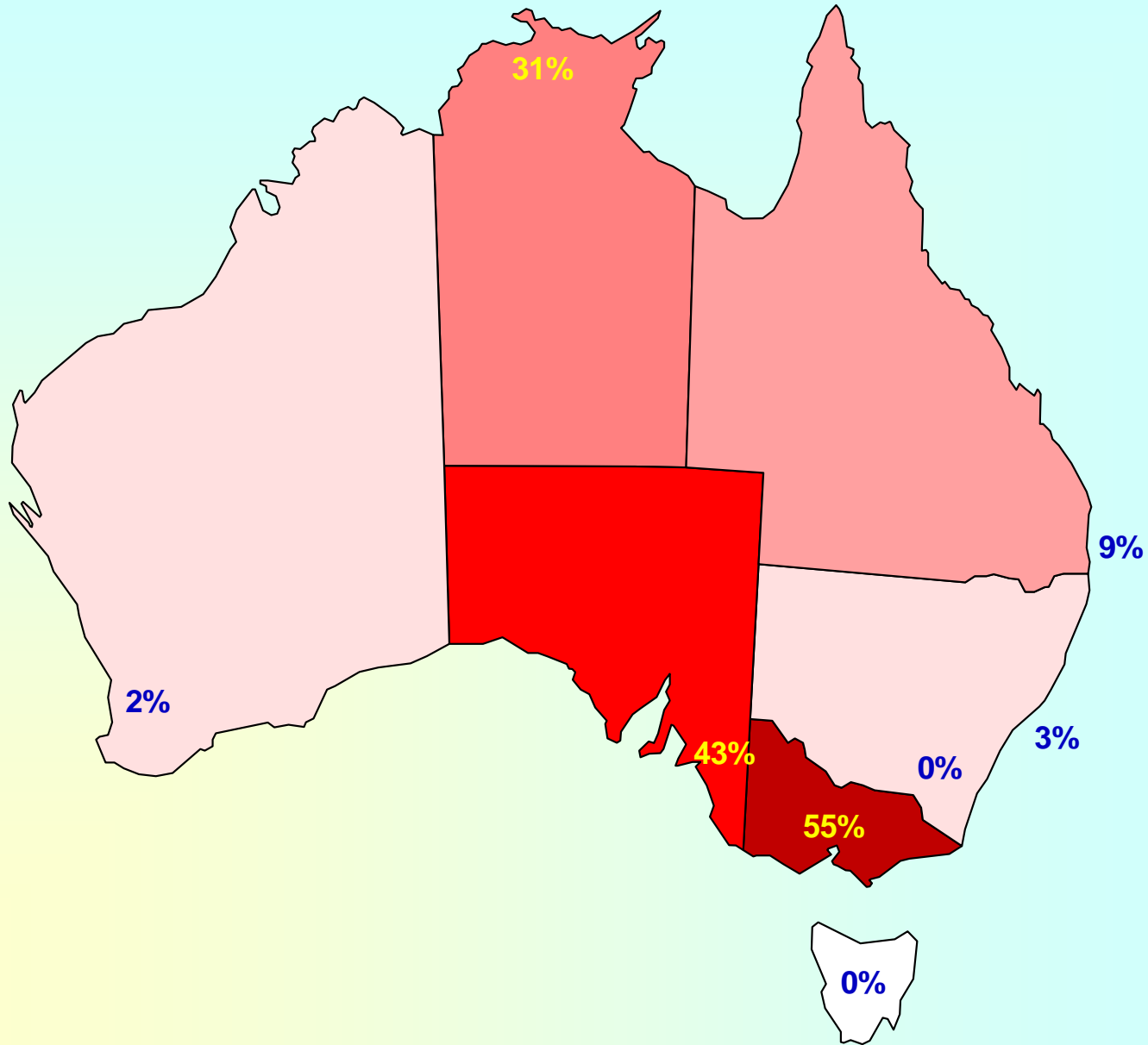
Where does Australia fit in the world MRSA epidemic?

- **Importer or exporter?**

Distribution of AUS-2 in 2001



Distribution of AUS-3 in 2001



Multiresistant Nosocomial MRSA in Australia

	Usually Resistant to	Urease	Phage susceptibility (typical)	Coagulase PCR/RFLP	MLST
AUS-1	Tet, Ery, Tmp, Gen, Chl, Hg, Pma	+	(84)/85/88A(90)	24	ST 239- MRSA-III
AUS-2	Tet, Ery, Tmp, Gen, Cip	+	85/88/90//47T/87M/MR8/MR12/M3	24	ST 239- MRSA-III
AUS-3	Tet, Ery, Tmp, Gen, Cip, HgCl ₂ , Pma	+	87M/M3	24	ST 239- MRSA-III

Advent of EA (AUS-1) MRSA?

- Hospital MRSA resistant to Ery, Tet, Gen, Tmp reported in Melbourne, 1976
- Increasing isolation of mrMRSA in Victorian hospitals from 1977
- Appearance of new strain of mrMRSA in Sydney in early 1980s
- Spread of 'EA MRSA' to UK in 1981 (UK EMRSA-1)
- ANS46 (RM4) - clinical isolate, 1982

Perceval et al MJA 1976;2:74 Bennett MJA 1985;142:138-9

Givney et al J Clin Microbiol 1998;36:552-6

Townsend et al J Hosp Infect 1987; 9:60-71

Matthews et al J Gen Microbiol 1987;138:169-80



‘Brazilian/Hungarian’ Clone



- Synonyms: EMRSA-1, -4, -11, Portugal/Brazil, Vienna

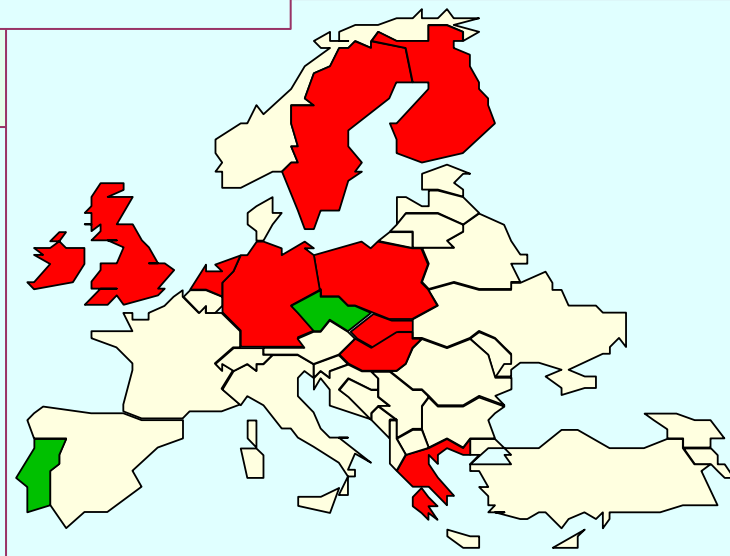
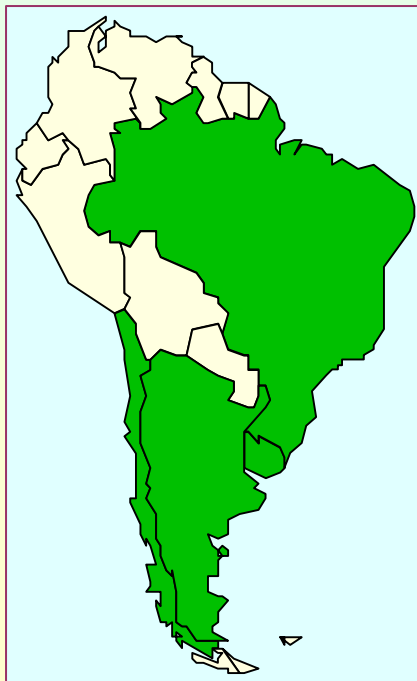
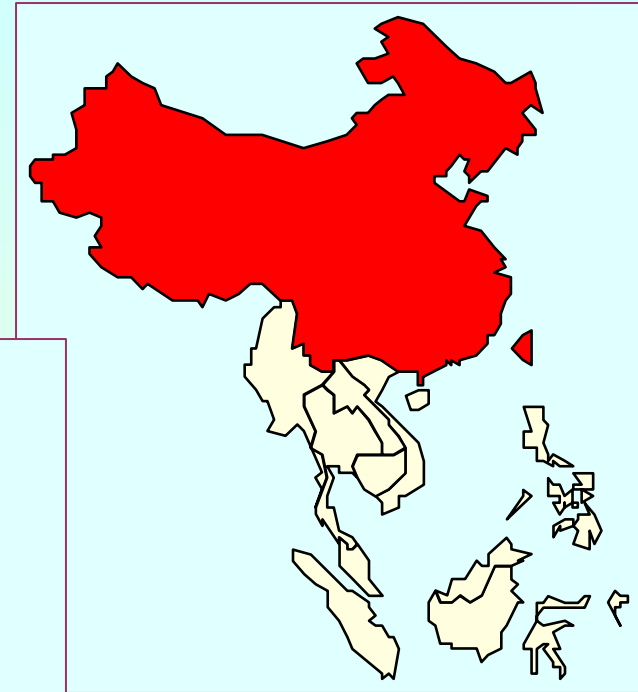
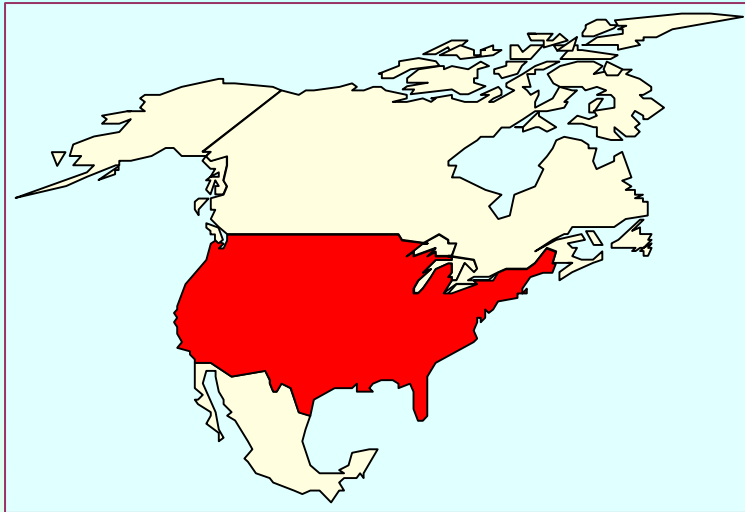
	Isolation year	MLS type	ST	SCCmec type	spaA type
Brazil ¹	1993	2-3-1-1-4-4-3	239	IIIA	WGKAOMQ
Hungarian ^{1,2}	1993	2-3-1-1-4-4-3	239	III	variableKAOMQ
Taiwan ³	1998	2-3-1-1-4-4-30	241	III	WGKAOMQ
China ³	1998	2-3-1-1-4-4-3	239	III	WGKAOMQ
Australia					
ANS46 ³	1982	2-3-1-1-4-4-3	239	III	WGKAOMQ
AGAR SAP	2000	2-3-1-1-4-4-3	239	?	?

1. Oliveira et al Microb Drug Resist 2001; 7:349-61
2. Enright et al PNAS 2002; 99:7687-92
3. Aires de Sousa et al J Clin Microbiol 2003; 41:159-63

'Brazilian/Hungarian'

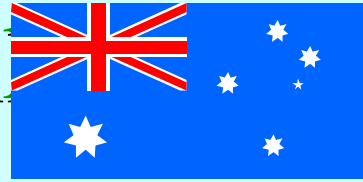


Clone





‘Brazilian Hungarian’ Clone



- Synonyms: EMRSA-1, -4, -11, Portugal/Brazil, Vienna

	Isolation year	MLS type	ST	SCCmec type	spaA type
Brazil ¹	1993	2-3-1-1-4-4-3	239	IIIA	WGKAOMQ
Hungarian ^{1,2}	1993	2-3-1-1-4-4-3	239	III	variableKAOMQ
Taiwan ³	1998	2-3-1-1-4-4-30	241	III	WGKAOMQ
China ³	1998	2-3-1-1-4-4-3	239	III	WGKAOMQ
Australia					
ANS46 ³	1982	2-3-1-1-4-4-3	239	III	WGKAOMQ
AGAR SAP	2000	2-3-1-1-4-4-3	239	?	?

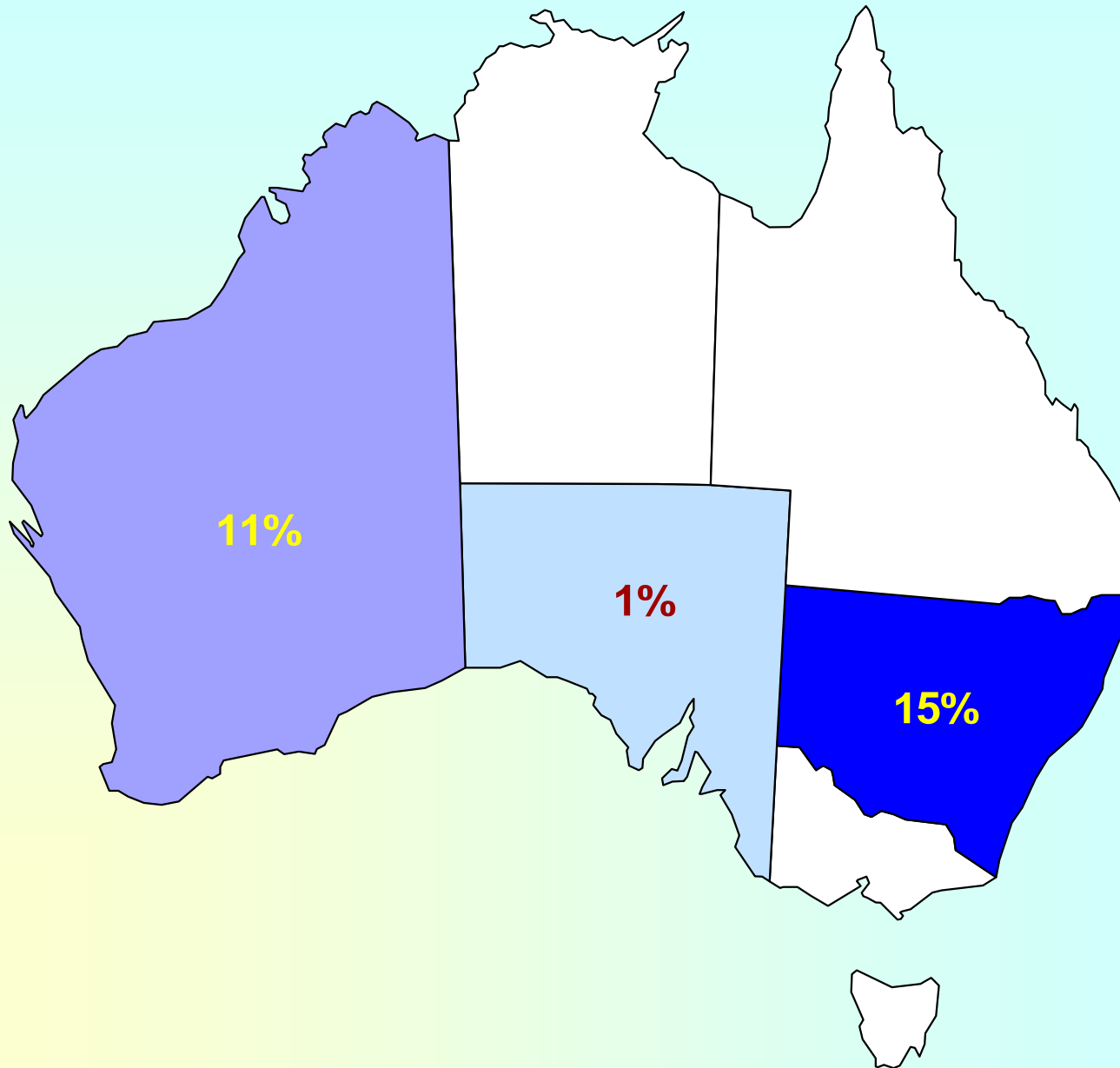
- ANS46 (RM4) - clinical isolate 1982

1. Oliveira et al Microb Drug Resist 2001; 7:349-61

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3. Aires de Sousa et al J Clin Microbiol 2003; 41:159-63

Distribution of UK EMRSA-15 in 2001



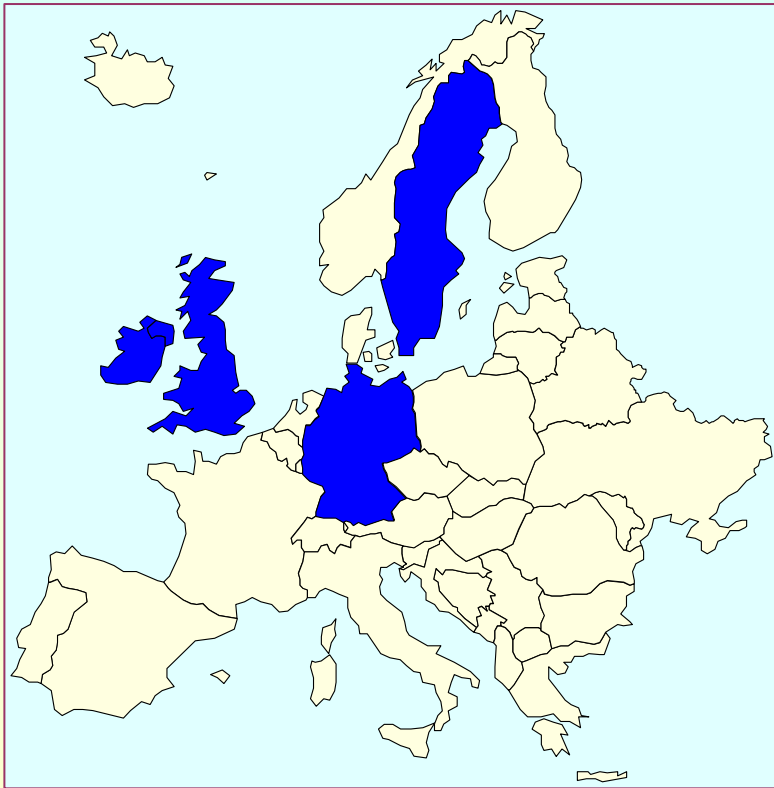
UK EMRSA-15

- Synonym: Barnim

	Isolation year	MLS type	ST	SCCmec type
Europe	various	7-6-1-5-8-8-6	22	IV
Australia AGAR SAP	2000	7-6-1-5-8-8-6	22	?

Enright et al PNAS 2002; 99:7687-92

UK EMRSA-15



MRSA in Australia- 5 Waves?

- ‘archaic’ or ‘classical’ MRSA, Sydney 1965-72
- ‘EA MRSA’ or ‘AUS1’, epidemic of multiresistant nosocomial MRSA in eastern and southern Australia (→ AUS2 and AUS3)
- ‘WA MRSA’, epidemic of community non-multiresistant MRSA in isolated WA then Perth then other states
- ‘WSPP’ or ‘SWP MRSA’, epidemic of community-acquired non-multiresistant MRSA in eastern Australia
- ‘UK EMRSA-15’, epidemic of nosocomial, non-multiresistant MRSA predominantly in NSW and WA

Conclusions

- MRSA is still a major problem in Australian hospitals
- Australian MRSA ‘epidemic’ is multiple epidemics of distinct strains, some multiresistant and some non-multiresistant
- These strains behave differently clinically and epidemiologically
- ‘Sporadic’ strains appear to be quite common (why?)