Corso di formazione e aggiornamento
ROTTURA PREMATURA DELLE MEMBRANE: pPROM

VERONA - 20 OTTOBRE 2012

Il punto di vista del neonatologo: ovvero del neonato l'epidemiologia degli esiti

Daniele Merazzi

The management of preterm premature rupture of the membranes near the limit of fetal viability

Thaddeus P. Waters, MD; Brian M. Mercer, MD

TABLE 2
Characteristics of pregnancies with PROM near viability

INCIDENZA: 4‰

Reference	n	GA at PROM (wk)	Mean GA at PROM (SD)	Mean maternal age (y)	Antibiotics (%)	Steroids (%)	Tocolytic (%)
Xiao et al[11,a]	28	14–24	21.6 (2.5)	–	Yes (89.3)	Yes (75.0)	–
Grisaru-Granovsky[8,b]	25	16–24	22.7 (1.0)	–	Yes (88.0)	Yes (60.0)	Yes (12.0)
Falk et al[13]	57	14–24	20.3 (n/a)	31.8 (n/a)	Yes (12.3)	Yes (33.3)	Yes (7.0)
Dinsmoor et al[10,c]	43	16–24	22.0 (median)	30.3 (7.0)	Yes (86.0)	Yes (n/a)	No
Muris et al[9,d]	49	18–24	21.1 (n/a)	29.3 (n/a)	Yes (69.4)	Yes (28.6)	Yes (14.3)
Everest et al[6,e]	98	<24	19.8 (2.5)	–	Yes (n/a)	Yes (97.5)	–

GA, gestational age; *n/a*, not applicable; *PROM*, premature rupture of membranes.

[a] Data reported for 28 liveborn infants admitted to neonatal intensive care department; [b] Ampicillin and erythromycin were given from admission to delivery, antenatal steroids were given at 24 wk and repeated at 28 wk, indomethacin was given for tocolysis if indicated; [c] Three declined expectant management, betamethasone was given routinely at 24 wk, antibiotics were given on admission; [d] Includes 20 terminations, ampicillin given on admission, betamethasone given routinely at 22 wk and repeated weekly; [e] Data reported only for 40 liveborn with latency ≥14 d, erythromycin given on admission, antenatal steroids given at 24 wk.

Waters. The management of PROM of the membranes near the limit of fetal viability. Am J Obstet Gynecol 2009.

AJOG 2009 September

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TABLE 3

Latency after conservatively managed PROM

Reference	GA at PROM (wk)	Mean GA at PROM (wk)	Mean GA at delivery (wk)	Mean latency (d)
Xiao et al[11,a]	14–24	21.6 (2.5)	27.1 (2.1)	39.4 (23.9)
Grisaru-Granovsky[8]	16–24	22.7 (1.0)	–	15.6 (n/a)
Falk et al[13]	14–24	20.3 (n/a)	–	6.0[b]
Dinsmoor et al[10]	16–24	22.0[b]	25.8 (3.4)	13.0[b]
Muris et al[9,c]	18–24	21.1 (n/a)	23.2 (n/a)	14.1 (n/a)

GA, gestational age; *n/a*, not applicable; *PROM*, premature rupture of membranes.

[a] Data reported for 28 liveborn infants admitted to neonatal intensive care department; [b] Median; [c] Outcomes for only 29 who did not terminate (n = 20) on presentation.

Waters. The management of PROM of the membranes near the limit of fetal viability. Am J Obstet Gynecol 2009.

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TABLE 5
Perinatal mortality after conservatively managed PROM

Reference	Mean GA at delivery (wk)	Stillbirth, n (%)	Liveborn, n (%)	Neonatal death, n (%)	Survival, n (%)
Xiao et al[11]	27.1 (2.1)	–[a]	–	12 (42.9)	16 (57.1)
Grisaru-Granovsky[8]	–	–	–	17 (68.0)	8 (32.0)
Falk et al[13,b]	–	30 (52.6)	27 (47.4)	12 (21.1)	15 (26.3)
Dinsmoor et al[10]	25.8 (3.4)	13 (22.8)	44 (77.2)	17 (29.8)	27 (47.4)
Muris et al[9]	23.2 (n/a)	–	–	–	12 (41.4)
Everest et al[6]	79	18 (22.8)	61 (77.2)	15 (19.0)	44 (55.7)
Total	275	61/193 (31.6)	132/193 (68.4)	73/246 (29.7)	122/275 (44.4)

TABLE 6
Survival after conservatively managed PROM

Reference	GA at PROM (wk)	PROM <22 wk (%)	PROM ≥22 wk (%)
Xiao et al[11,a]	14–24	2/11 (18.1)	14/17 (82.4)
Grisaru-Granovsky[8]	16–24	2/10 (20.0)	5/15 (33.3)
Falk et al[13,b]	14–24	4/37 (10.8)	11/20 (55.0)
Total		8/57 (14.4)	30/52 (57.7)

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SOPRAVVIVENZA: è importante notare che i dati pubblicati tendono a sovrastimare la sopravvivenza neonatale poiché vengono escluse quelle gravidanze non elegibili per un trattamento conservativo (corionamniosite) o quelle che hanno optato per un trattamento attivo basandosi sulla prognosi.

Il normale sviluppo polmonare avviene in 5 fasi:

Embrionale

Pseudoghiandolare

6 – 17 settimane

PROM perivitale

Canalicolare

16 – 26 settimane

Sacculare

25 – 37 settimane

Alveolare

> 36 settimane – 18 mesi

Nella fase canalicolare si sviluppano i bronchioli terminali e i pneumociti di II tipo. Raramente un oligoamnios dopo PROM > 26 settimane esita in un'ipoplasia polmonare letale.

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TABLE 7

Neonatal morbidity and mortality after conservative management of premature rupture of membranes near the limit of viability

Reference	n	Pulmonary hypoplasia, n (%)	RDS, n (%)	BPD, n (%)	Sepsis, n (%)	IVH grade III-IV, n (%)	ROP stage III, n (%)	NEC, n (%)	Contractures, n (%)	Hospital duration (d, mean)	Intact survival
Xiao et al[11]	28	7 (25.0)	12 (42.9)	8 (17.9)	5 (17.9)	1 (3.6)	–	–	–	–	10/13[a] (76.9)
Grisaru-Granovsky[8]	25	3 (12.0)	5 (20.0)	–	5 (20.0)	2 (8.0)	2 (8.0)	1 (4.0)	0 (0.0)	–	–
Falk et al[13]	27	3 (11.1)	–	–	3 (11.1)	–	–	–	2 (7.4)	–	–
Dinsmoor et al[10]	35[b]	–	29 (82.9)	8 (22.9)	12 (34.3)	4 (11.4)	–	–	–	71 (median)	17/27[c] (63.0)
Muris et al[9]	12[d]	–	10 (83.3)	–	5 (41.7)	0 (0.0)	–	–	0 (0.0)	27.4	–
Everest et al[6]	40[e]	10 (25.0)	36 (90.0)	14 (35.0)	1 (2.5)	0 (0.0)	1 (2.5)	–	–	–	–
Total	167	23/120 (19.2)	92/140 (65.7)	30/103 (29.1)	31/167 (18.6)	7/140 (5.0)	3/65 (4.6)	1/25 (4.0)	2/64 (3.1)		27/40 (67.5)

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IPOPLASIA POLMONARE: in molti casi riportati dalla letteratura non viene eseguita l'autopsia perciò gli autori danno una definizione clinica di ipoplasia polmonare che non è sempre attendibile. L'esatta incidenza di questa complicanza, che viene riportata tra il 9 e il 20% dei neonati con PROM perivitale, è quindi verosimilmente sottostimata.

Epoca gestazionale alla PROM, durata della latenza, quantità di liquido amniotico residuo.

LIQUIDO AMNIOTICO E IPOPLASIA POLMONARE

Oligoamnios PERSISTENTE

(dopo PROM 14 – 24 sett)

SENSIBILITA' 52 -100%

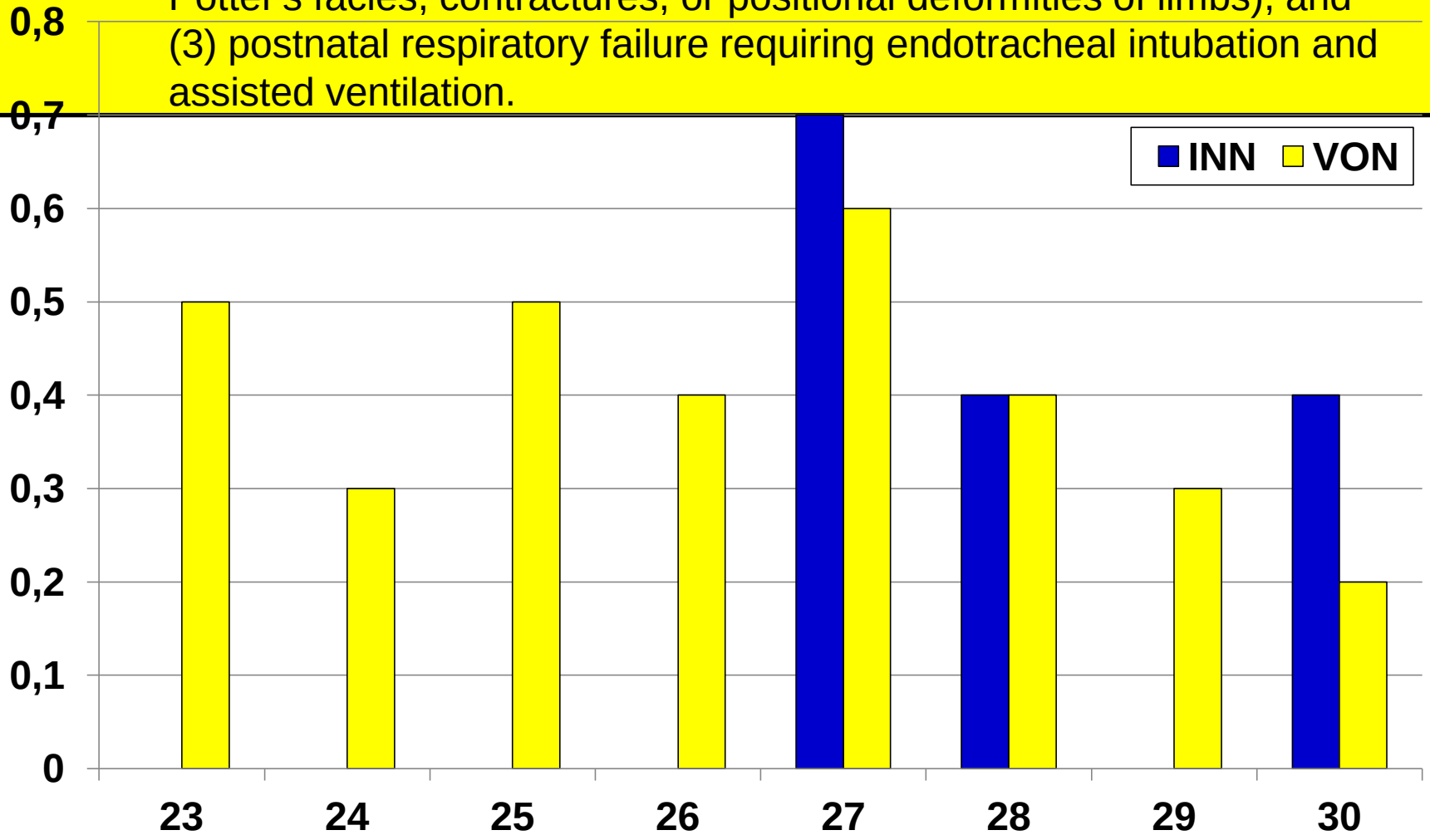
SPECIFICITA' 41 – 82%

VPP 22 – 64%

VPN 89 - 100%

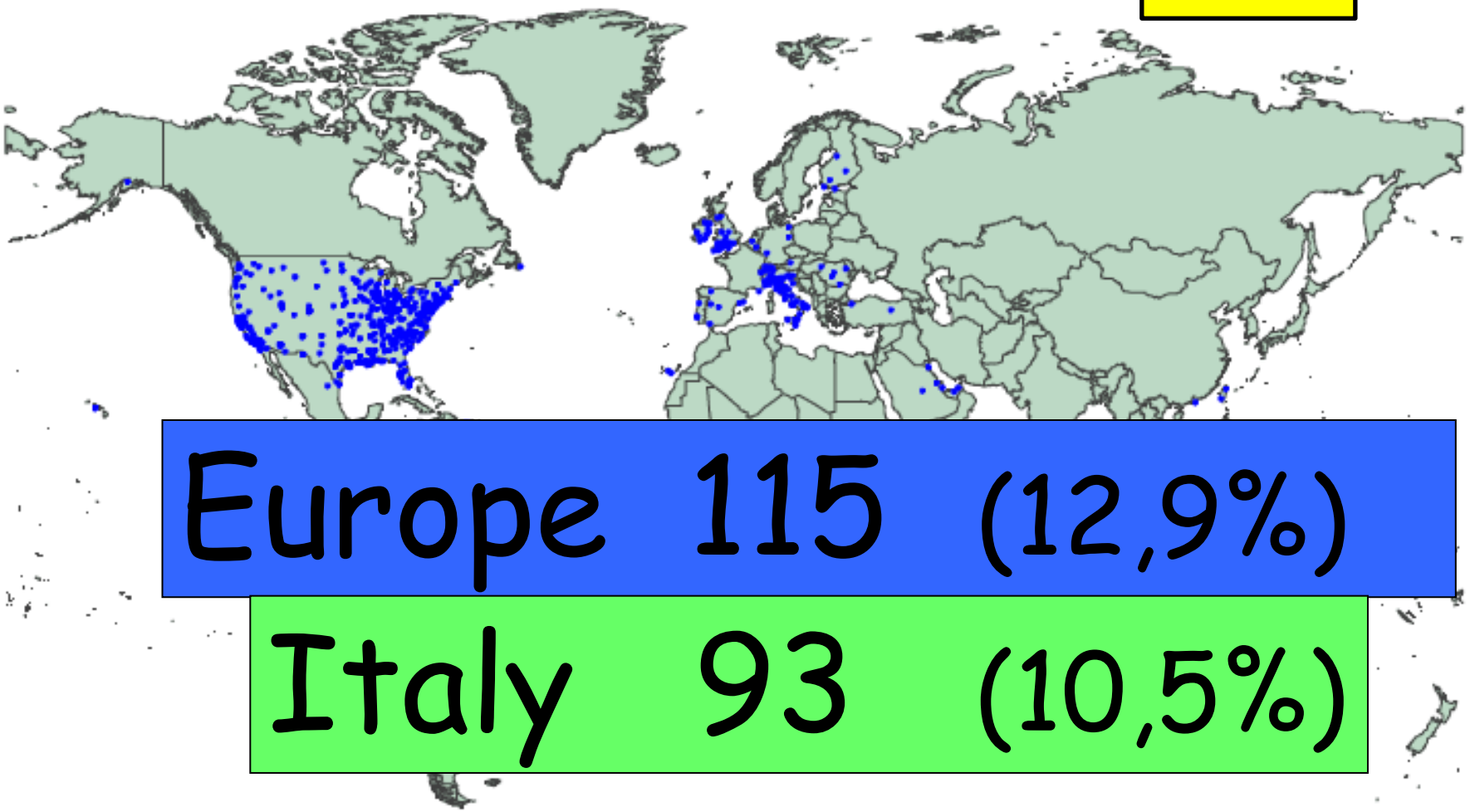
Oligohydramnios sequence

Description Oligohydramnios sequence including all 3 of the following:
(1) Oligohydramnios documented by antenatal ultrasound 5 or more days prior to delivery,
(2) evidence of fetal constraint on postnatal physical exam (such as Potter's facies, contractures, or positional deformities of limbs), and
(3) postnatal respiratory failure requiring endotracheal intubation and assisted ventilation.



Vermont Oxford Network Members, 2012

889



Europe 115 (12,9%)

Italy 93 (10,5%)

The vision of the Vermont Oxford Network is to establish a worldwide community of practice, dedicated to providing all newborn infants and their families with the best possible perinatal and neonatal care.

GEOGRAPHIC DISTRIBUTION OF MEMBER CENTERS 2012

	N	%
United States		
Region		
New England	21	3
Middle Atlantic	76	9
East North Central	94	12
International		
Country		
Austria	9	1
Belgium	1	0
Brazil	4	0
Canada	5	1
Namibia	1	0
Portugal	4	0
Romania	1	0
Saudi Arabia	2	0
Singapore	1	0
Slovenia	1	0
South Africa	37	5
Spain	10	1
Turkey	1	0
United Arab Emirates	4	0
United Kingdom	23	3
Total International	199	24
Total All Hospitals	812	100

Europe 115 (11%)

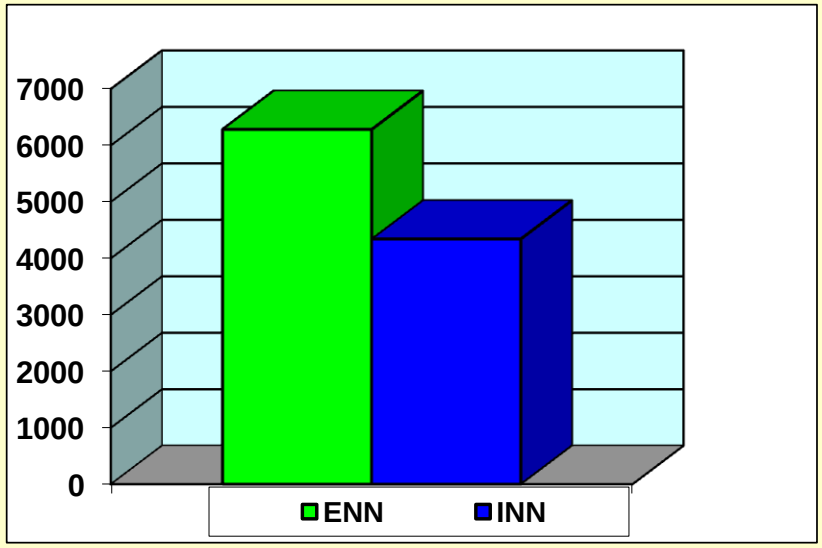
Italy 93(11%)

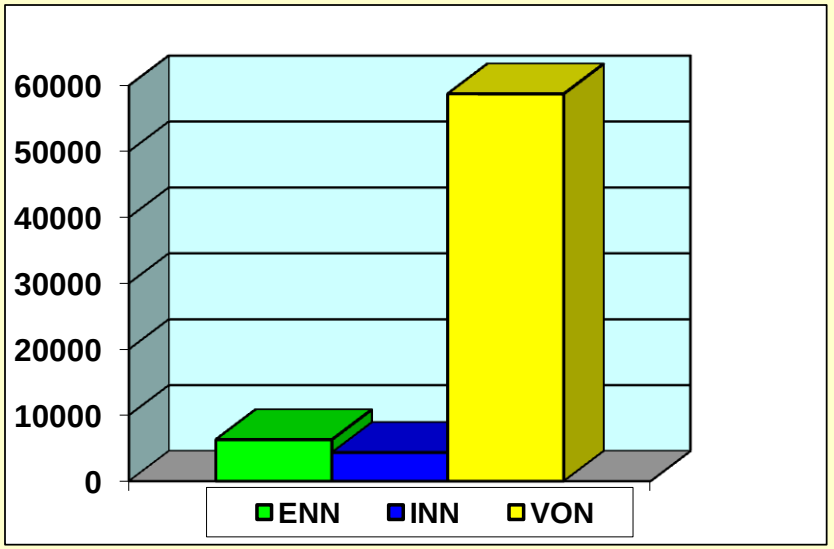
Numero di VLBW o EG < 30 wk - 2011

Vermont Oxford Network (VON **889**) n= 59.946

European Neonatal Network (ENN **115**) n= 6.283 **(10,5%)**

Italian Neonatal Network (INN **93** **[10,5%]**) n= 4.342 **(7,2%)** **[69%]**





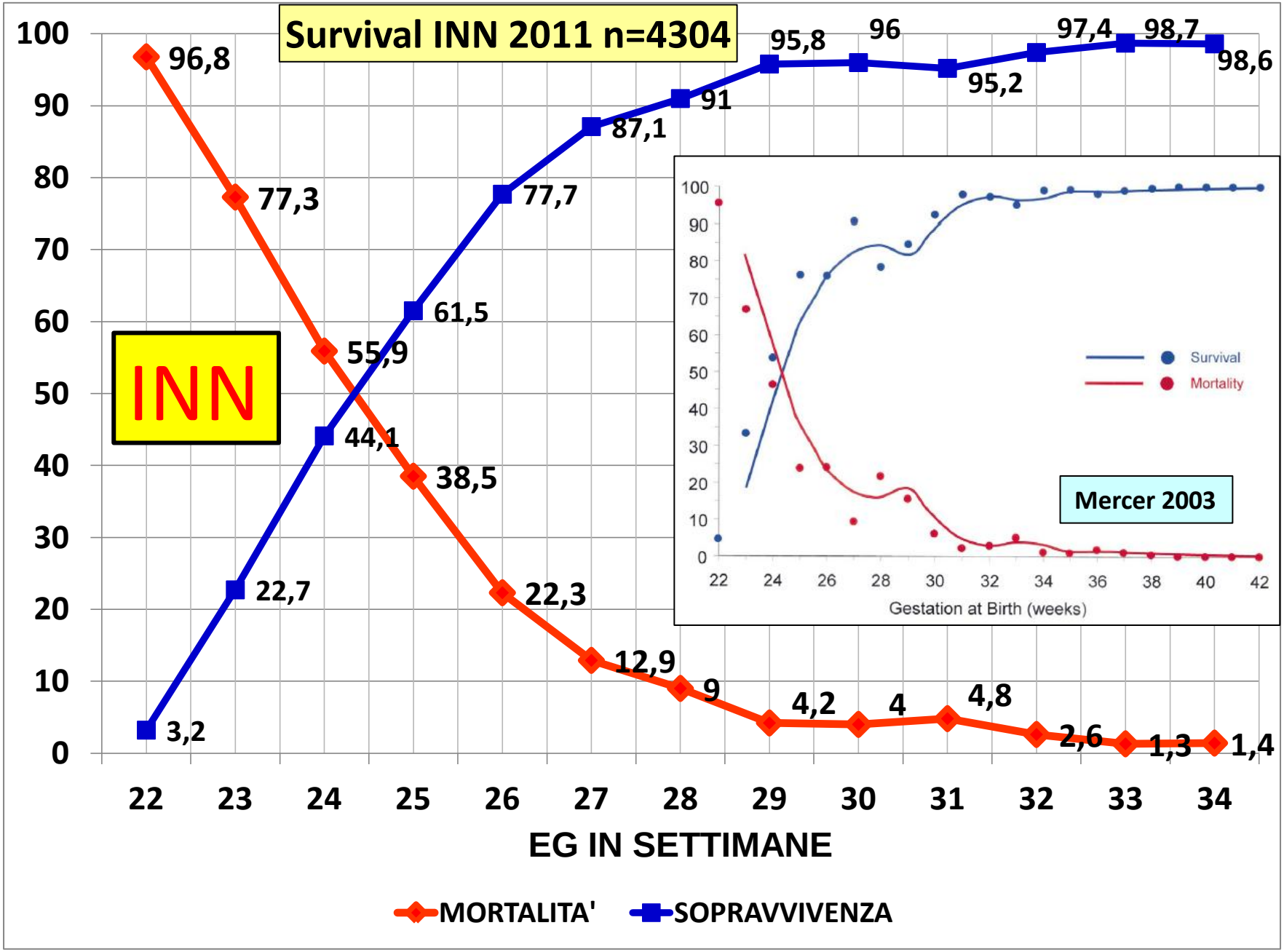
Vermont Oxford Network 2011 INN Group Report

Table 7.1, Admissions by Gestational Age
Infants 501 to 1500 Grams, Born in 2011

	INN Group		Network	
	N	%	N	%
All	4,180	100.00	56,212	100.00
< 24 Weeks	140	3.35	2,547	4.53
24-26 Weeks	720	17.22	13,189	23.46
27-29 Weeks	1,424	34.07	20,594	36.64
30-32 Weeks	1,411	33.76	15,558	27.68
> 32 Weeks	485	11.60	4,322	7.69

Qual è la probabilità di un neonato di 27 settimane, nato in Italia di sopravvivere ?

a. 75 %
b. 87 %
c. 95 %
d. 43 %
e. 62 %


Survival INN 2011 n=4304
INN
96,8
77,3
55,9
38,5
22,3
12,9
9
4,2
4
4,8
2,6
1,3
1,4
3,2
22,7
44,1
61,5
77,7
87,1
91
95,8
96
95,2
97,4
98,7
98,6
100
90
80
70
60
50
40
30
20
10
0
22
23
24
25
26
27
28
29
30
31
32
33
34
EG IN SETTIMANE
MORTALITA'
SOPRAVVIVENZA
Survival
Mortality
Mercer 2003
Gestation at Birth (weeks)
22
24
26
28
30
32
34
36
38
40
42

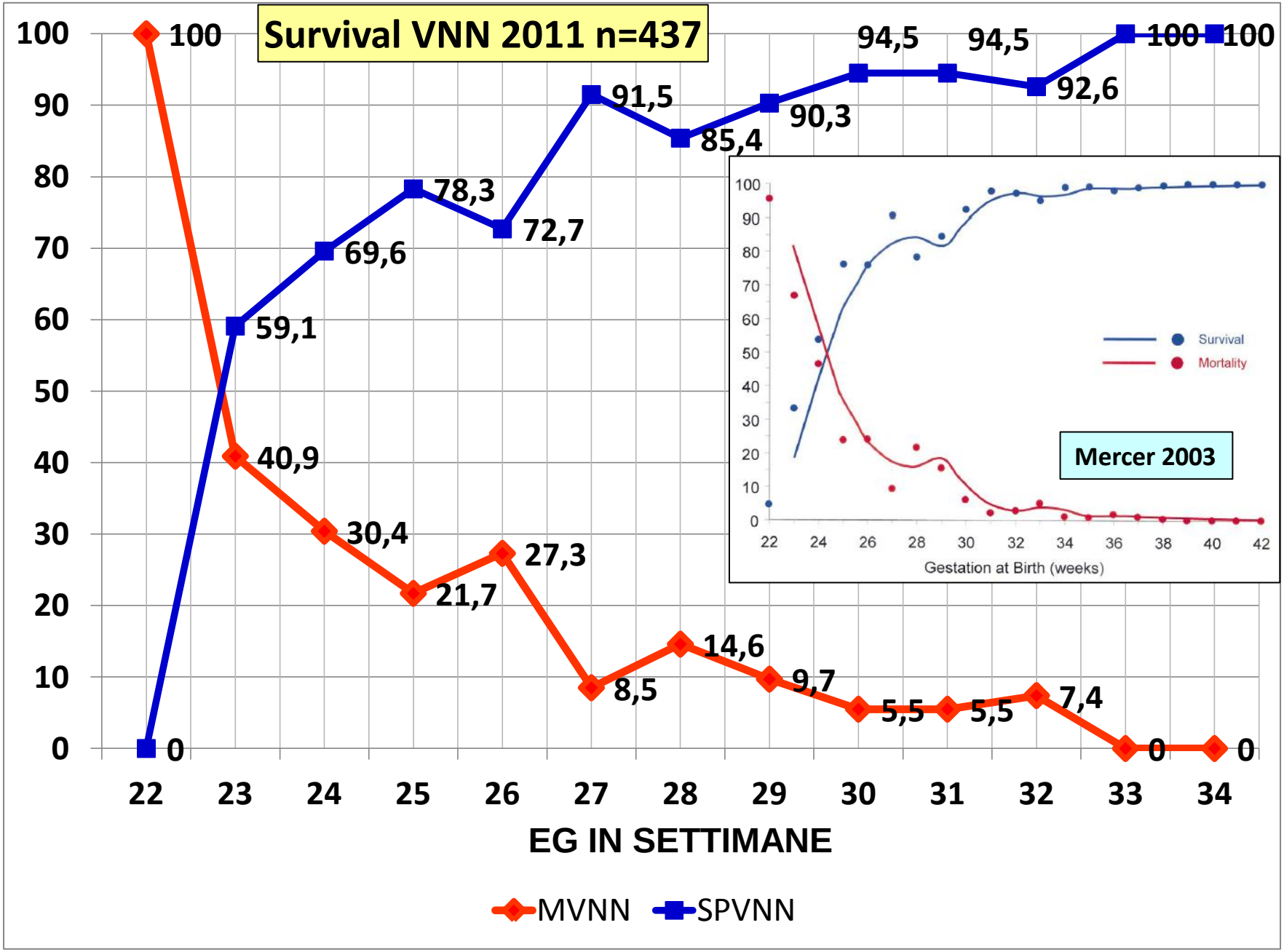
Qual è la probabilità di un neonato di 27 settimane, nato in Italia di sopravvivere ?

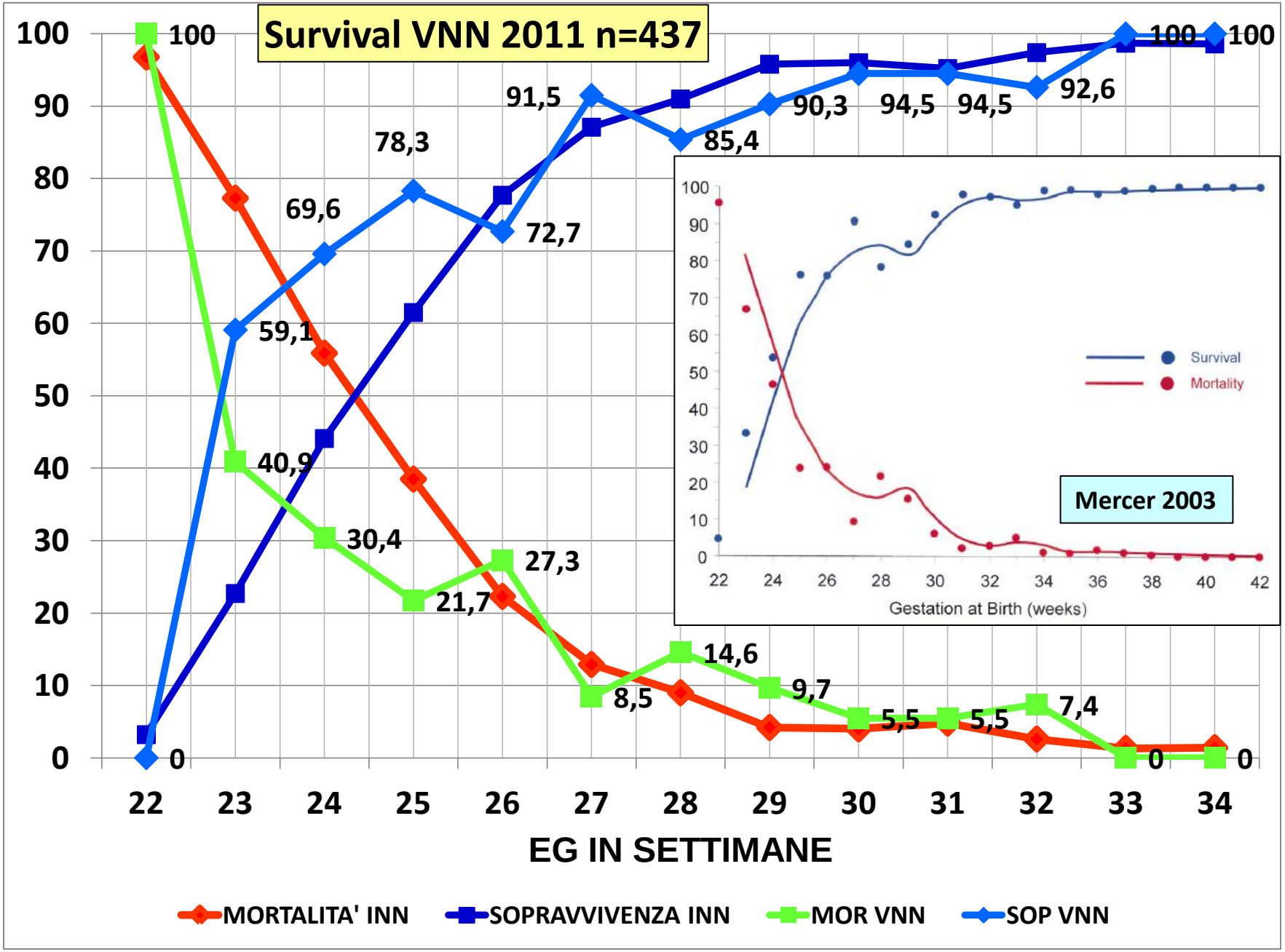
a.	75 %
b.	**87 %**
c.	95 %
d.	43 %
e.	62 %

Vermont Oxford Network 2011 INN Group Report
Centers Participating in INN Group

Hospital	City
Az.Ospedaliera Universitaria Integrata	Verona-OCM Verona
NICU Pediatric Department, University of Padua	Padua
Ospedale di Santorso	Santorso (VI)
Patologia Neonatale Ca Foncello Hospital,Treviso	Treviso
Patologia Neonatale Camposampiero	Camposampiero
Patologia Neonatale Ospedale San Bortolo	Vicenza
Policlinico G. B. Rossi	Verona

VENETO NEONATAL NETWORK
2011 = 437 vlbw


Survival VNN 2011 n=437
100
90
80
70
60
50
40
30
20
10
0
22
23
24
25
26
27
28
29
30
31
32
33
34
EG IN SETTIMANE
MVNN
SPVNN
100
40,9
30,4
21,7
27,3
8,5
14,6
9,7
5,5
5,5
7,4
0
0
0
59,1
69,6
78,3
72,7
91,5
85,4
90,3
94,5
94,5
92,6
100
100
Survival
Mortality
Gestation at Birth (weeks)
Mercer 2003


Survival VNN 2011 n=437
100
90
80
70
60
50
40
30
20
10
0
22
23
24
25
26
27
28
29
30
31
32
33
34
EG IN SETTIMANE
100
0
69,6
59,1
40,9
30,4
21,7
27,3
8,5
14,6
9,7
5,5
5,5
7,4
0
0
78,3
91,5
72,7
85,4
90,3
94,5
94,5
92,6
100
100
MORTALITA' INN
SOPRAVVIVENZA INN
MOR VNN
SOP VNN
Survival
Mortality
Mercer 2003
Gestation at Birth (weeks)

Qual è la probabilità di un neonato di 25 settimane, nato in Italia di sopravvivere senza morbilità specifiche ?

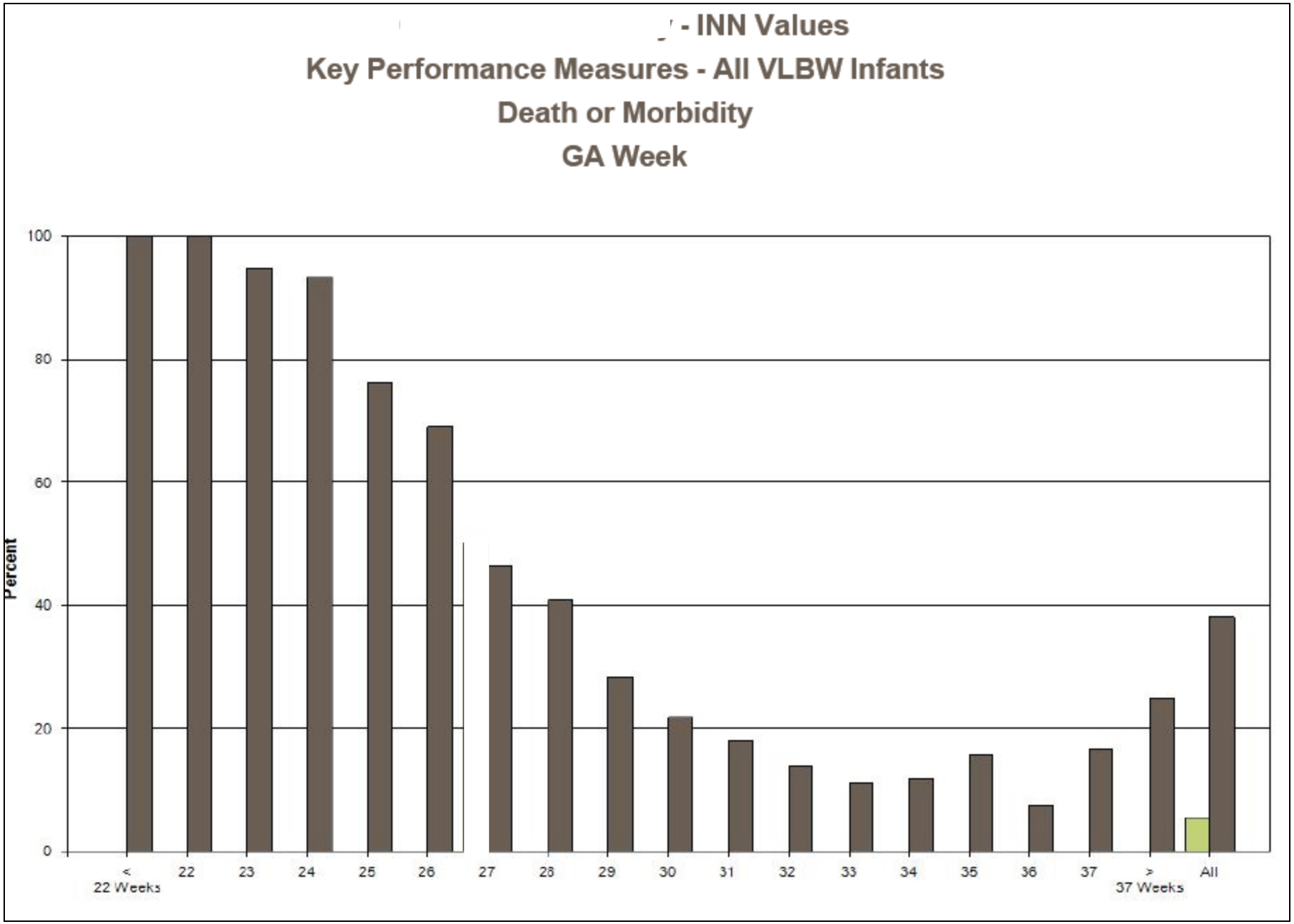
a. 32 %
b. 55 %
c. 25 %
d. 10 %

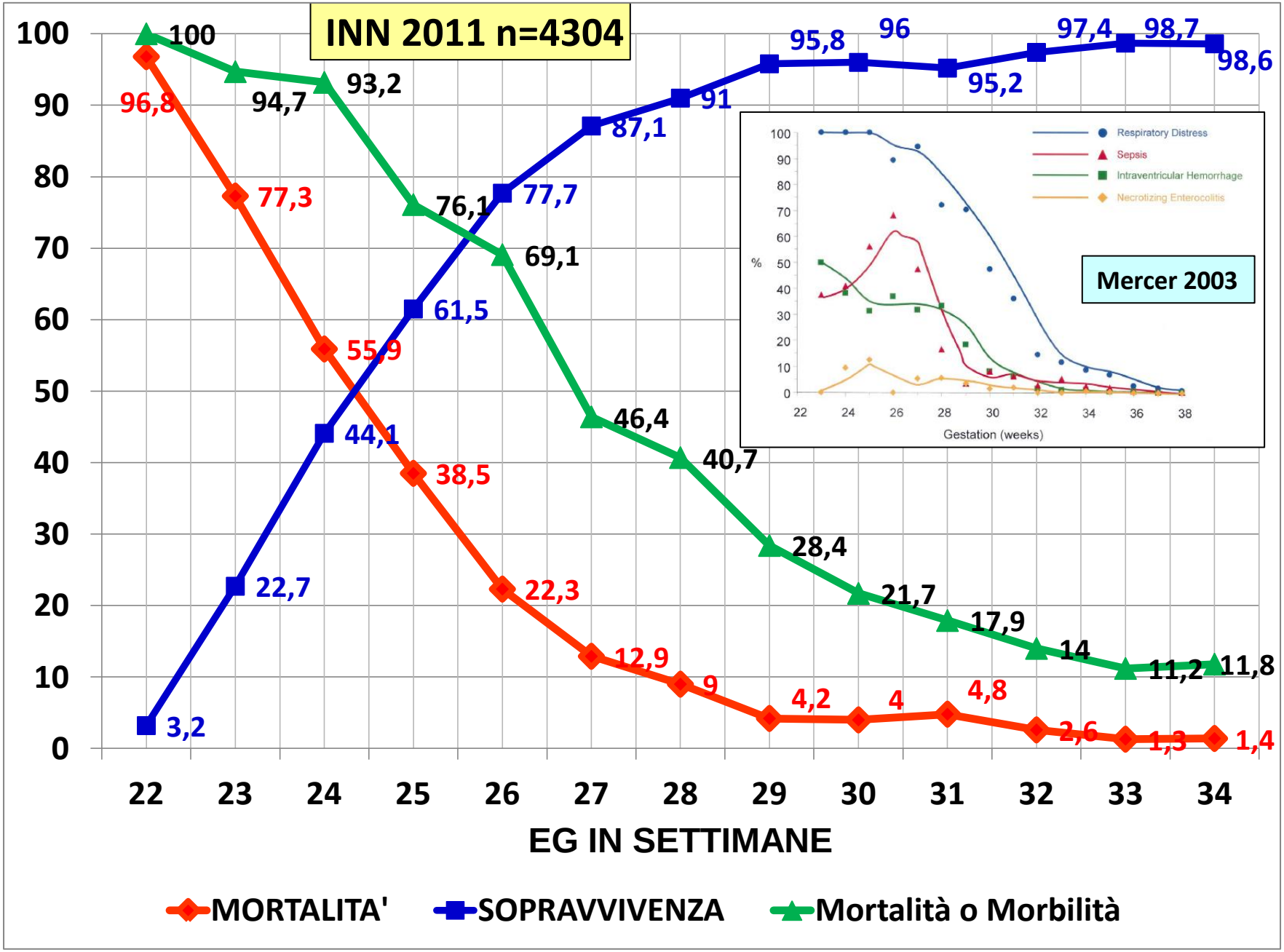
Mortalità o Morbilità
Network INN - VON 2011

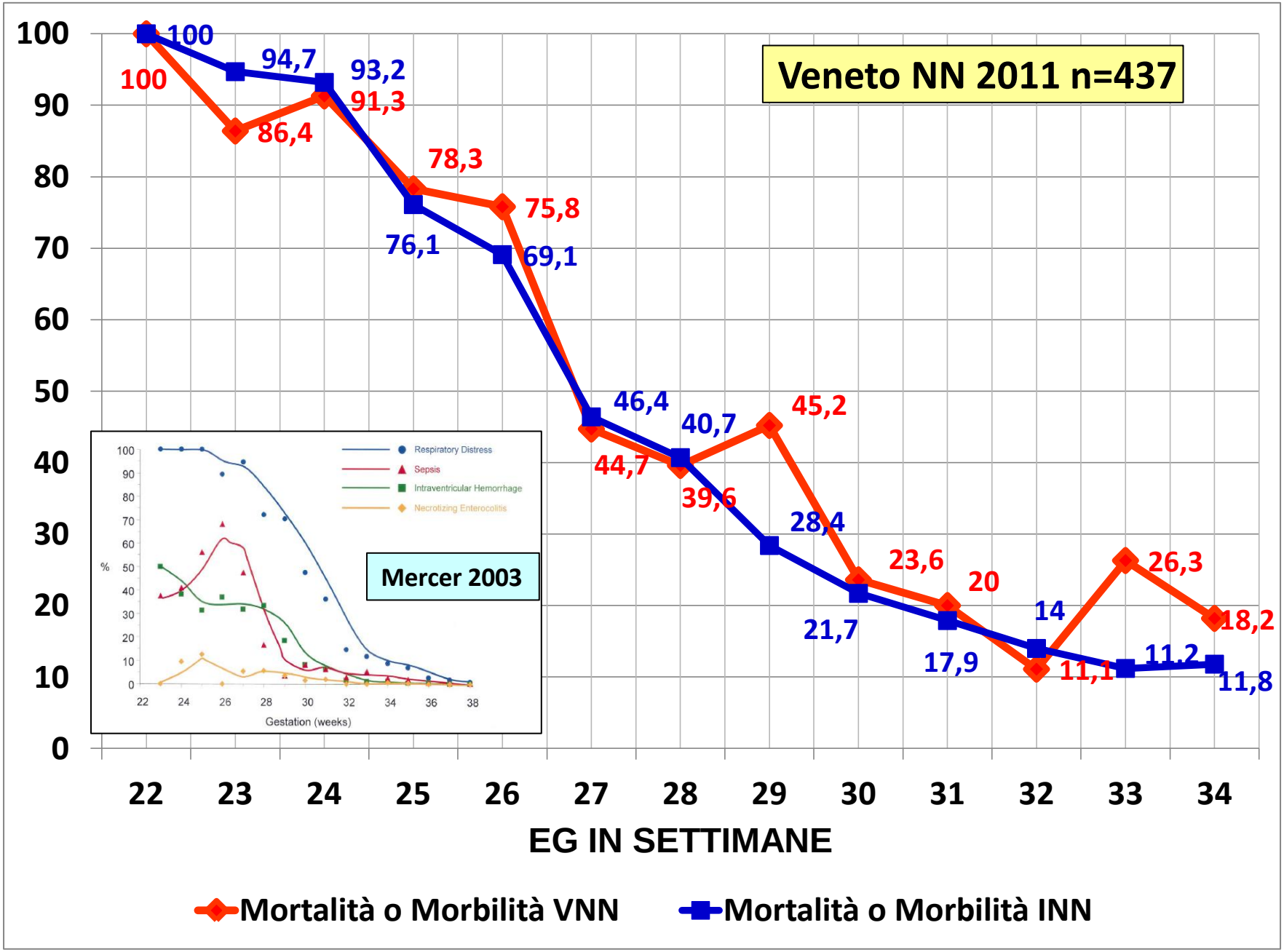
Death or Morbidity

Definition: Indicates whether the infant died or is known to have had one or more of the following key morbidities:

Severe IVH,
CLD,
NEC,
Pneumothorax,
Any Late Infection,
PVL


- INN Values
Key Performance Measures - All VLBW Infants
Death or Morbidity
GA Week
Percent
100
80
60
40
20
0
< 22 Weeks
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
> 37 Weeks
All


INN 2011 n=4304
100
90
80
70
60
50
40
30
20
10
0
22
23
24
25
26
27
28
29
30
31
32
33
34
EG IN SETTIMANE
96,8
77,3
55,9
38,5
22,3
12,9
9
4,2
4
4,8
2,6
1,3
1,4
3,2
22,7
44,1
61,5
77,7
87,1
91
95,8
96
95,2
97,4
98,7
98,6
100
94,7
93,2
76,1
69,1
46,4
40,7
28,4
21,7
17,9
14
11,2
11,8
Respiratory Distress
Sepsis
Intraventricular Hemorrhage
Necrotizing Enterocolitis
%
Gestation (weeks)
Mercer 2003
MORTALITA'
SOPRAVVIVENZA
Mortalità o Morbilità


Veneto NN 2011 n=437
100
94,7
93,2
76,1
69,1
46,4
40,7
28,4
21,7
17,9
14
11,2
11,8
100
86,4
91,3
78,3
75,8
44,7
39,6
45,2
23,6
20
11,1
26,3
18,2
Mercer 2003
Respiratory Distress
Sepsis
Intraventricular Hemorrhage
Necrotizing Enterocolitis
%
Gestation (weeks)
EG IN SETTIMANE
Mortalità o Morbilità VNN
Mortalità o Morbilità INN

Qual è la probabilità di un neonato di 25 settimane, nato in Italia di sopravvivere senza morbilità specifiche ?

a. 32 %

b. 55 %

c. 25 %

d. 10 %

TAKE HOME MESSAGES

- Counselling congiunto perinatologico
- Conoscenza epidemiologica regionale e locale
- Condivisione delle indicazioni comportamentali tra centri
- Promuovere network Perinatologico

ITALIAN PERINATAL NETWORK