

AAB 2014
Annual Meeting and Educational Conference
International Perspective on IVF

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Disclosures

- **Industry**
 - Advanced Reproductive Care (ARC): Founder and CEO
- **Professional Organizations**
 - ASRM: Past President
 - FIGO: Chair, Reproductive Medicine Committee
 - ICMART: Int'l Committee Monitoring ART
 - IFFS: Executive Committee
 - WERF: President
 - WHO: Co-chair, Reproductive Committee
- **Funded Research Studies/Consultant**
 - Auxogyn
 - Bayer
 - LabCorp

ICMART

International Committee
Assisted Reproductive Technologies

David Adamson: USA
Fernando Zegers: Chile
Elizabeth Sullivan: Australia
Karl Nygren: Sweden
Osamu Ishihara: Japan
Ragaa Mansour: Egypt
Jacques de Mouzon: France
Manish Banker: India
Silke Dyer: South Africa

ICMART is an NGO in official relations with WHO.



World Health
Organization

The International Committee Monitoring Assisted Reproductive Technologies (ICMART)



- An independent, **international** non-profit organization
- Taken a **leading** role in
- Development, collection and dissemination of **worldwide data on ART**
- Provides information on **access, effectiveness and safety**
- To health professionals, health authorities and the public



Data Collection on Outcomes and Adverse Effects Helps

- **Patients** make informed decisions
- Medical Profession and Laboratory **Professionals** in providing optimal patient care
- **Public Health** Authorities developing health care delivery and reimbursement policies
- The **Public** in understanding ART better

Different Levels and Purposes of ART Data Collection

- **Individual centers**
 - Monitoring own procedures
 - Research
 - Information for patients
 - Basis for publication
- **National and regional registries**
 - Summarize total experience of all ART clinics

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Different Levels and Purposes of ART Data Collection

- **International data collection** programs
 - Generally multicenter **epidemiologic** studies rather than a multinational registry program
 - International data collection and analysis for **research** studies primarily serves to identify rare but very important events
- **International registry**
 - Describe the worldwide use of ART
 - Access, effectiveness, safety
 - Identify **similarities, differences and trends**

Access to Reproductive Health Care



Millennium Development Goal 5b “Universal access to reproductive health”

- Inter American Court of Human Rights 2012
 - Costa Rica’s ban of ART violates human rights and discriminates against poor
 - Reparations include access to ART through public health systems
 - Costa Rica government resisting



Data Collection Methodology

- National collection and analysis of **clinic result summaries**
 - Inexpensive and simple
 - Each center gives a yearly summary report
 - Disadvantage is that it is **less informative**
- Centralized data collection from **all cycles** started in **all centers** within one country
 - More difficult and expensive
 - Requires a uniform data system
 - Opportunities for **research** on multiple factors influencing selected outcomes of interest

ICMART World Reports on ART

- ICMART World Report on Assisted Reproductive Technology **2007**. Submitted for publication. Fertil Steril.
- ICMART World Report on Assisted Reproductive Technology **2006**. In press. Hum Reprod.
- ICMART World Report on Assisted Reproductive Technology **2005**. Fertil Steril. 2014 Feb;101(2):366-78. doi: 10.1016/j.fertnstert.2013.10.005. Epub 2013 Nov 1.
- ICMART World Report on Assisted Reproductive Technology **2004**. Hum Reprod; 2013 May; 28 (5): 1375-1390.
- ICMART World report: assisted reproductive technology **2003**. Fertil Steril 2011; 95(7): 2209-2222.e17.
- ICMART World Collaborative Report on Assisted Reproductive Technology, **2002**. Hum Reprod 2009; 24(9): 2310-2320.
- ICMART, prepared by Adamson D, de Mouzon J (Coordinator), Lancaster P, Nygren KG (Chairman), Sullivan E and Zegers-Hochschild F. World collaborative report on in vitro fertilization **2000**. Fertil Steril 2006; 85:1586–1622.
- IWGROAR. World collaborative report on assisted reproductive technology, 1998. IFFS, Melbourne, 25–29 November 2001a.
- IWGROAR. World collaborative report on assisted reproductive technology, 1998. In: Healy DL, Kovacs GP, McLachlan E, Rodriduez-Armas O(eds). Reproductive Medicine in the 21st Century. London, UK: Parthenon Publishing Group, 2001b, 209–219.
- IWGROAR. World report: preliminary data for 1996. 16th World Congress on Fertility and Sterility, IFFS, San Francisco, USA, 4–9 October 1998.
- IWGROAR. World collaborative report on in vitro fertilization. Preliminary data for 1995. J Assist Reprod Gen 1997;14:251s–265s.
- IWGROAR. World collaborative report on in vitro fertilization, 1993. Congress Booklet, Montpellier, 17–22 September 1995, 1–43.
- IWGROAR. World collaborative report on in vitro fertilization, 1991. VIIIth Congress on In Vitro and Alternate Assisted Reproduction, Congress Booklet, **Kyoto,12–15 September 1993**, 1–38.

Other ICMART Publications

www.icmartivf.org

- Adamson GD, Lancaster P, de Mouzon J, Nygren KG & Zegers-Hochschild F. **A simple headstone** or just eliminate the chads? Letter to the Editor, Fertil Steril 2001; 76(6):1284-5.
- Adamson GD, Lancaster P, de Mouzon J, Nygren K, Sullivan E, Zegers-Hochschild F. ICMART World Report on In Vitro Fertilization 2000: **How Does the United States Compare?** Fertil Steril 2005; 84(S1), S86.
- Adamson GD, Zegers-Hochschild F, Nygren KG, de Mouzon J, Ishihara O. ICMART report on **global trends in ART** from 2000-2004: how does the USA compare? Fertil Steril 2009; 92(3), S1, S53
- Zegers-Hochschild F, Adamson GD, Nygren KG, de Mouzon J, Ishihara O. **Worldwide differences in access to assisted reproduction technology (ART) influence providers/consumers decisions on the number of embryos transferred**, affecting the proportion of multiple births. Fertil Steril 2009; 92(3), S1: S80-S81
- Nygren K, Adamson GD, Zegers-Hochschild F, de Mouzon J. **Cross-border fertility care** – International Committee Monitoring Assisted Reproductive Technologies global Survey: 2006 data and estimates. Fertil Steril 2010; 94(1):e4-e10.
- Adamson GD, Tabangin M, Macaluso M, de Mouzon J. The **number of babies** born globally after treatment with the assisted reproductive technologies (ART). Abstract presented at ASRM, October 14, 2013. In preparation.

ICMART/WHO Glossary

- Developed in cooperation with the **World Health Organization (WHO)**
- Facilitates dissemination of ART data through a set of **agreed-upon definitions**
- Provides a conceptual framework for further international terminology and **data development** for ART
- **Being revised 2014**

www.icmartivf.org

- **NEW!! The ICMART Tool Box for ART Data Collection**
- The ICMART Tool Box for ART Data Collection is a package to **facilitate** the monitoring and **data collection** of ART cycles and outcomes.

www.icmartivf.org

Pending ICMART Publications

- ICMART World Report on ART **2008.**
In preparation. Hum Reprod.
- ICMART World Report on ART **2009.**
Data analysis. Fertil Steril.
- ICMART World Report on ART **2010.**
Data collection. Hum Reprod.
 - **New data collection program**
 - **Directly online**
 - **Developed by ICMART with Uppsala University**

ART World Report 2009

■ Registers : Regional Organisations

- EUROPE : ESHRE : Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Rep, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Kazakhstan, Latvia, Lithuania, Macedonia, Moldova, Montenegro, Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovenia, Spain, Sweden, Switzerland, Ukraine , UK
- AUSTRALIA -NEW ZEALAND : Australia, New Zealand
- LATIN AMERICA : Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Guatemala, Mexico, Peru, Uruguay, Venezuela
- NORTH AMERICA : Canada, USA
- Middle-East : Egypt, Lebanon, Palestinian territory

■ Registers : National Level :

- Israel, Japan, Korea, South Africa
- Individual clinics: Cameroon, Togo, Tunisia

World Report 2009

Countries/Region

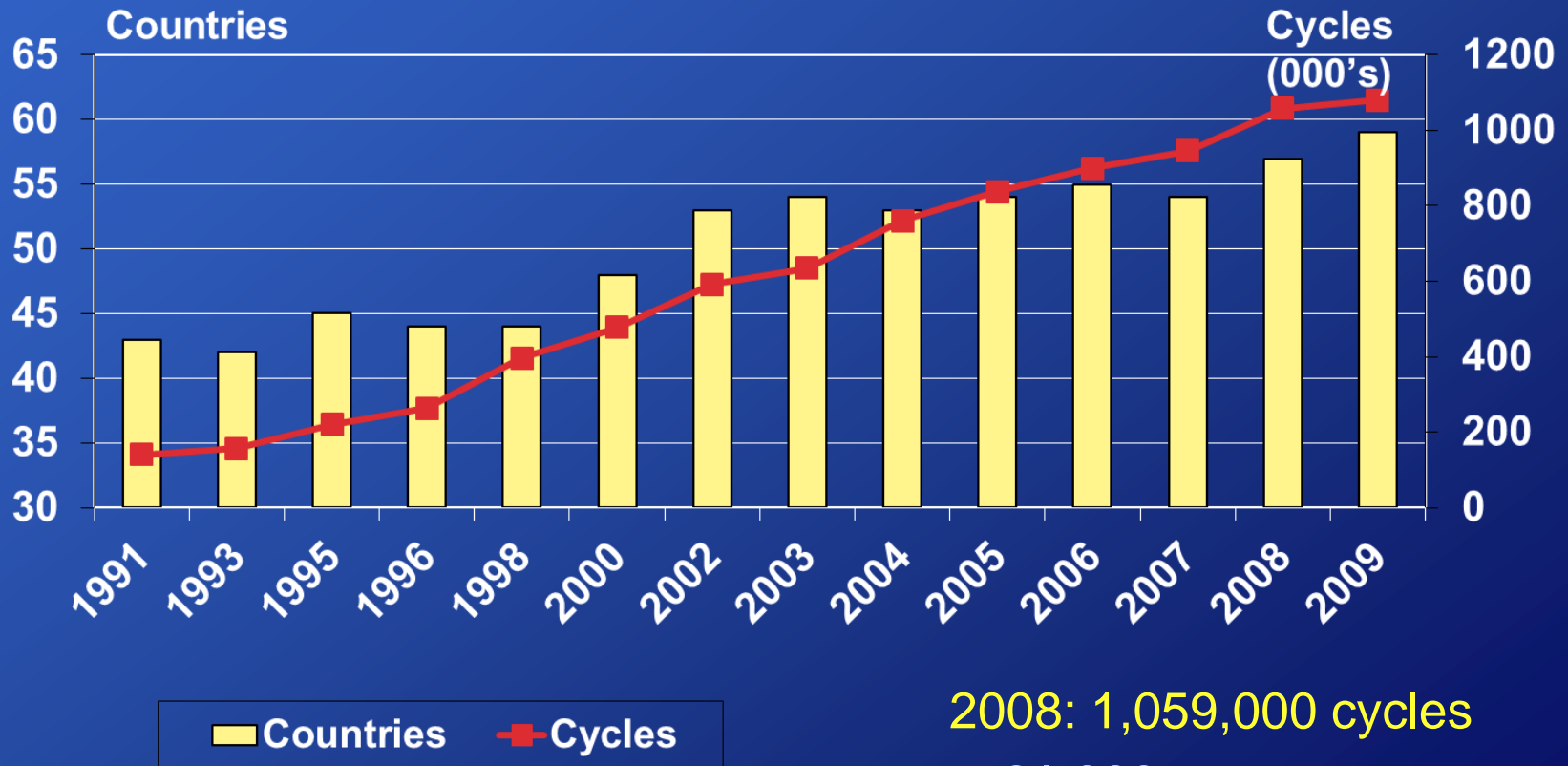
	Participating (n)
Africa	4
America, Latin	11
America, North	2
Asia	2
Australia-NZ	2
Europe	34
Middle East	3
Israel	1
Total	59

Access to ART



International Committee Monitoring
Assisted Reproductive Technologies

Number of Countries and Cycles Reported to ICMART



2008: 1,059,000 cycles
+ 21,000
2% increase

ARS Question 1: Which country performs the most IVF cycles in the world?

1. United States
2. United Kingdom
3. China
4. Japan
5. Unknown

Main Contributors 2009 (> 40,000 cycles)

TOTAL 1,080,479

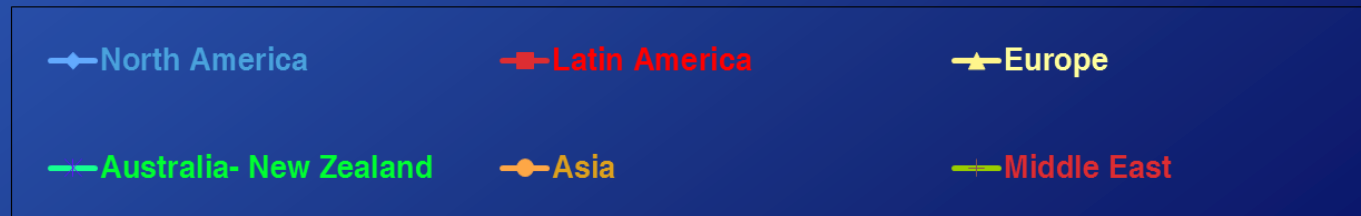
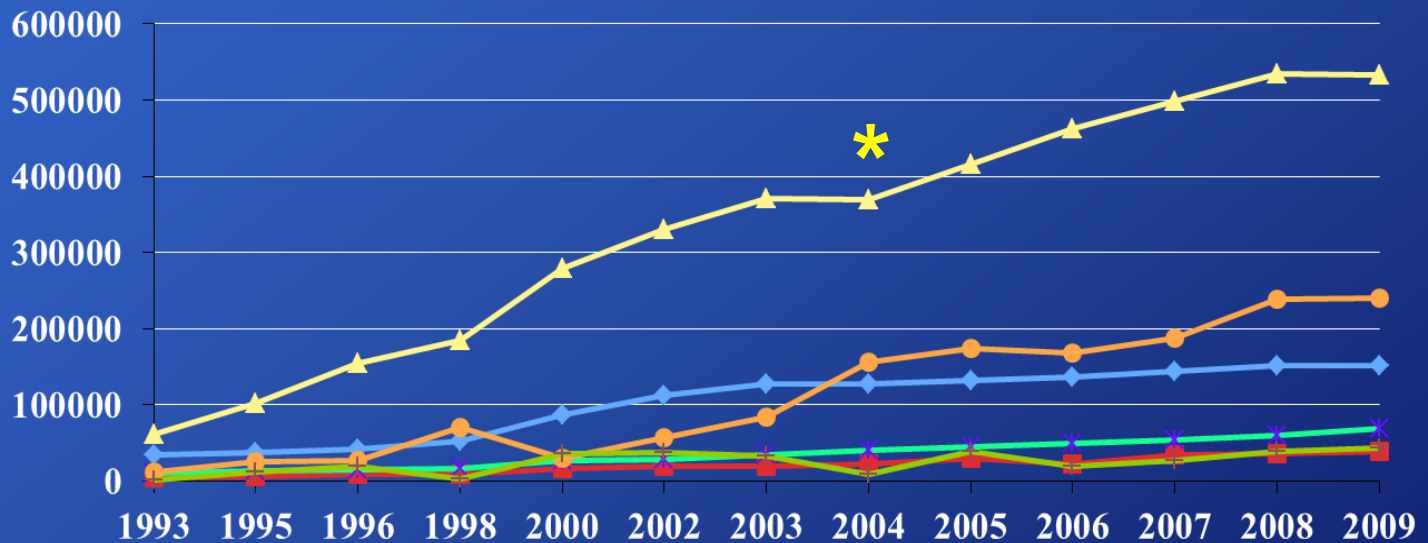
■ Japan	211,942
■ USA:	135,405
■ France	80,919
■ Germany	68,487
■ Australia	63,041
■ UK	54,069
■ Spain	53,717
■ Italy	48,930
■ Russia	40,834

70%

ICMART World Coverage 2009

- **59 countries** (25 in 1991, 57 in 2008)
 - Almost all Europe, Americas, Australia-NZ
 - Missing countries : Africa, Middle-East, Asia
 - But 4 new African countries (Cameroon, South Africa, Tunisia, Togo): hope for future ?
- **2,237 clinics : approximately 80 % of clinics**
 - **27 countries with full coverage**
- **Estimate of the overall coverage**
 - **63 % - 70 % of World activity**

Number of ART Cycles by Region

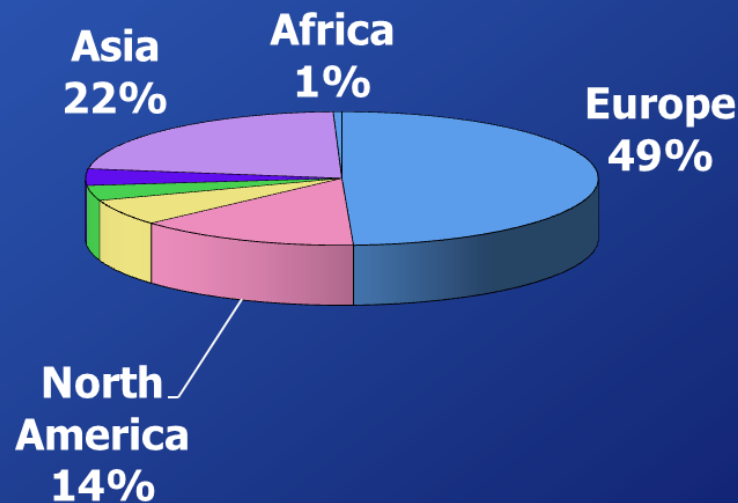


* In 2004, decrease of 40,000 German cycles because of law changing IVF funding.

Regional Contribution of ART Cycles to the World Report 2009

N = 1,080,479

Middle East	4%
Latin America	3%
Australia & New Zealand	6%



Corresponds to aspiration cycles in IVF, ICSI & GIFT and transfer cycles in FET & OD.

Number of ART Cycles According to Public/Private Health Expenditure 2006 (Zegers. ICMART)

GDP per capita (US\$ 2006)	National Health Exp. as % of GDP) (2006)	Public (%)	Private (%)	ART Cycles / 1,000,000 pop. (2004)
\$34,200 – 50,856	France (11.0%)	84.0	16.0	1062
	Denmark (10.8)	84.0	16.0	2008
	Sweden (9.2%)	81.2	18.8	1341
	UK (8.2%)	87.4	12.6	623
	Australia (8.7%)	67.2	32.8	1739
	Japan (8.1%)	82.2	17.8	890
\$43,000	USA (15.2%)	45.8	54.2	357
\$3,350 – 8,894	Argentina (10.1%)	45.5	54.5	125
	Brazil (7.5%)	47.7	52.1	56
	Mexico (6.6%)	43.3	56.7	34
	Chile (5.3%)	47.3	52.7	73
	Peru (4.4%)	42.9	57.1	26
\$1,512	Egypt (6.3%)	40.7	59.3	114
\$20,863	Israel (8.0%)	65.3	34.7	3541

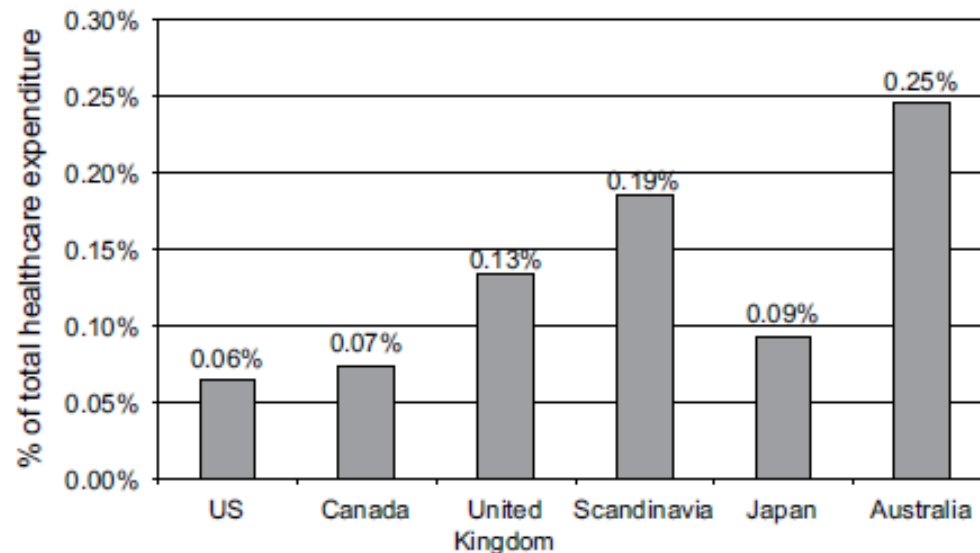
Access to ART (2004) According to Demographic Factors & Fertility Rate

Country / Region	Female median age (2006)	Total fertility rate (children per woman) (2000-2005)	Population Annual Growth Rate (2006)	Availability (cycles per million) (2004)
France	39.7	1.88	0.6	1062
Sweden	41.5	1.67	0.4	1341
Denmark	40.2	1.76	0.2	2008
UK	39.8	1.70	0.4	623
Japan	44.3	1.29	0.1	890
USA	37.4	2.04	1.0	357
Argentina	29.9	2.35	1.0	125
Brazil	27.7	2.35	1.3	56
Chile	30.8	2.00	1.0	73
Mexico	25.5	2.40	1.0	34
Peru	24.8	2.70	1.1	26
Egypt	23.8	2.91	1.8	114
Israel	29.0	3.17	1.7	3541

Total ART Treatment Costs as a Percentage of Total Healthcare Expenditure (USD 2006)

FIGURE 5

Total ART treatment costs as a percentage of total healthcare expenditure (USD 2003).



Note:

Total healthcare expenditure was sourced from The World Bank, World Development Indicators database (24).

Chambers. International economic review of ART. Fertil Steril 2009.

Profile of Procedures and Patients

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The background features a light blue world map at the top. Below it is a large, semi-transparent globe with the acronym 'ICMART' overlaid in the center. At the bottom, there is a thick, light blue wave-like graphic that curves across the page.

Global Results 2009

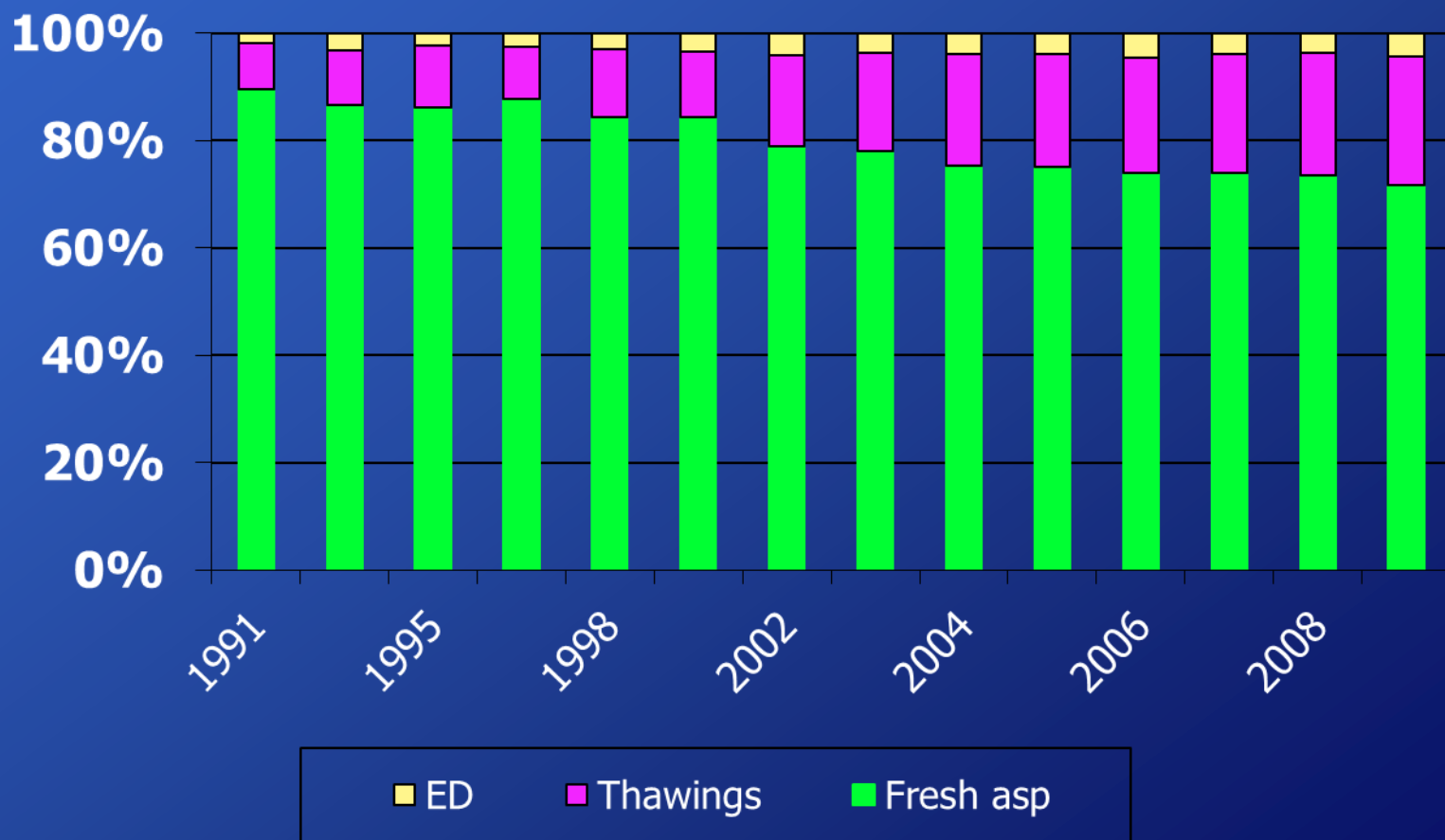
- 1,080,479 initiated cycles, 195,873 deliveries

■ 731,703 aspirations		Delivery Rate
■ 200,713	IVF*	
■ 432,545	ICSI**	22.6%
■ 334	GIFT	
■ 242,519	Thaws	18.7%
■ 10,695	PGD/PGS	9.5%
■ 44,671	Egg donations	33.1%

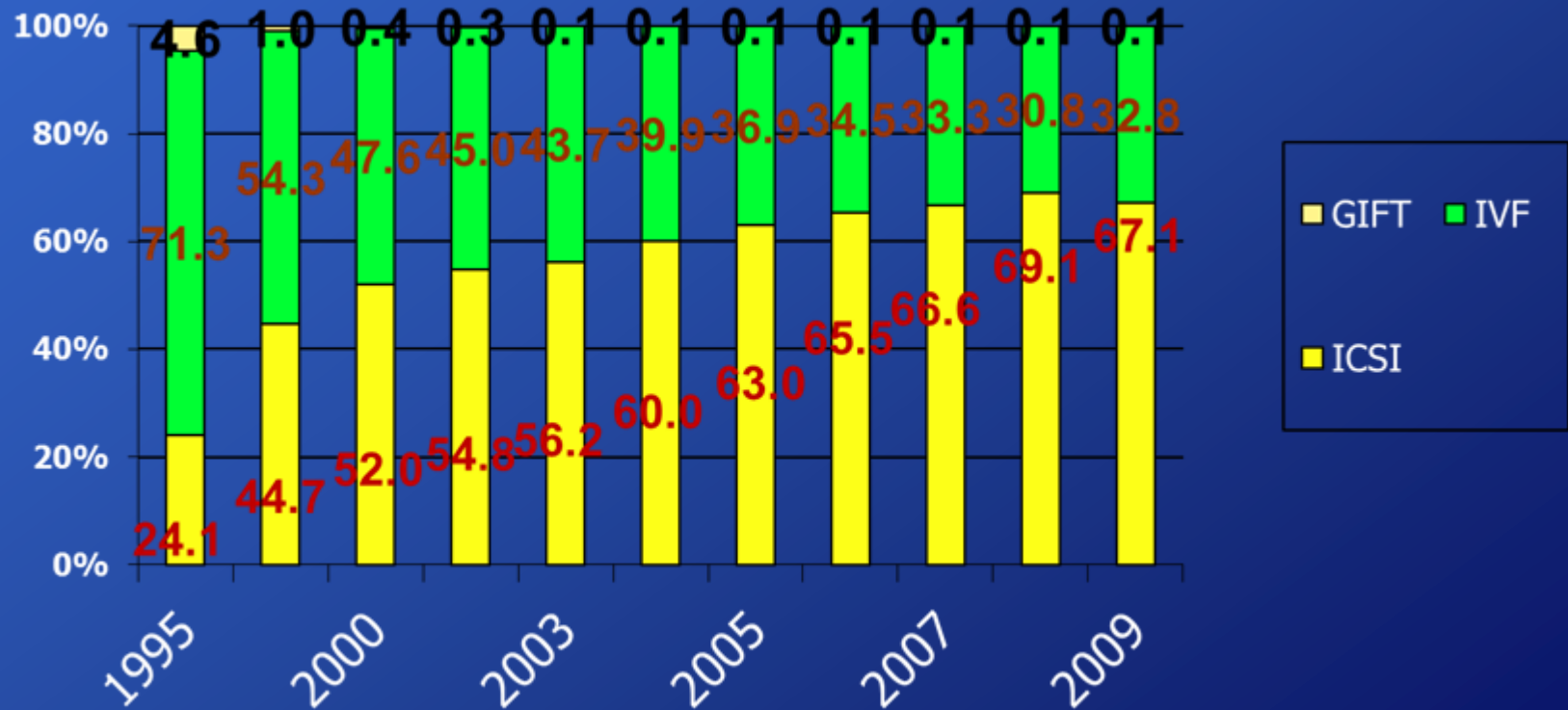
*Not counted: Japan IVF aspirations for **freezing only** 22,924; Israel retrieval sum of IVF & ICSI 21,862; Australia 35,875; NZ 2,895.

**Not counted: Japan: ICSI aspirations for freezing only 32,424.

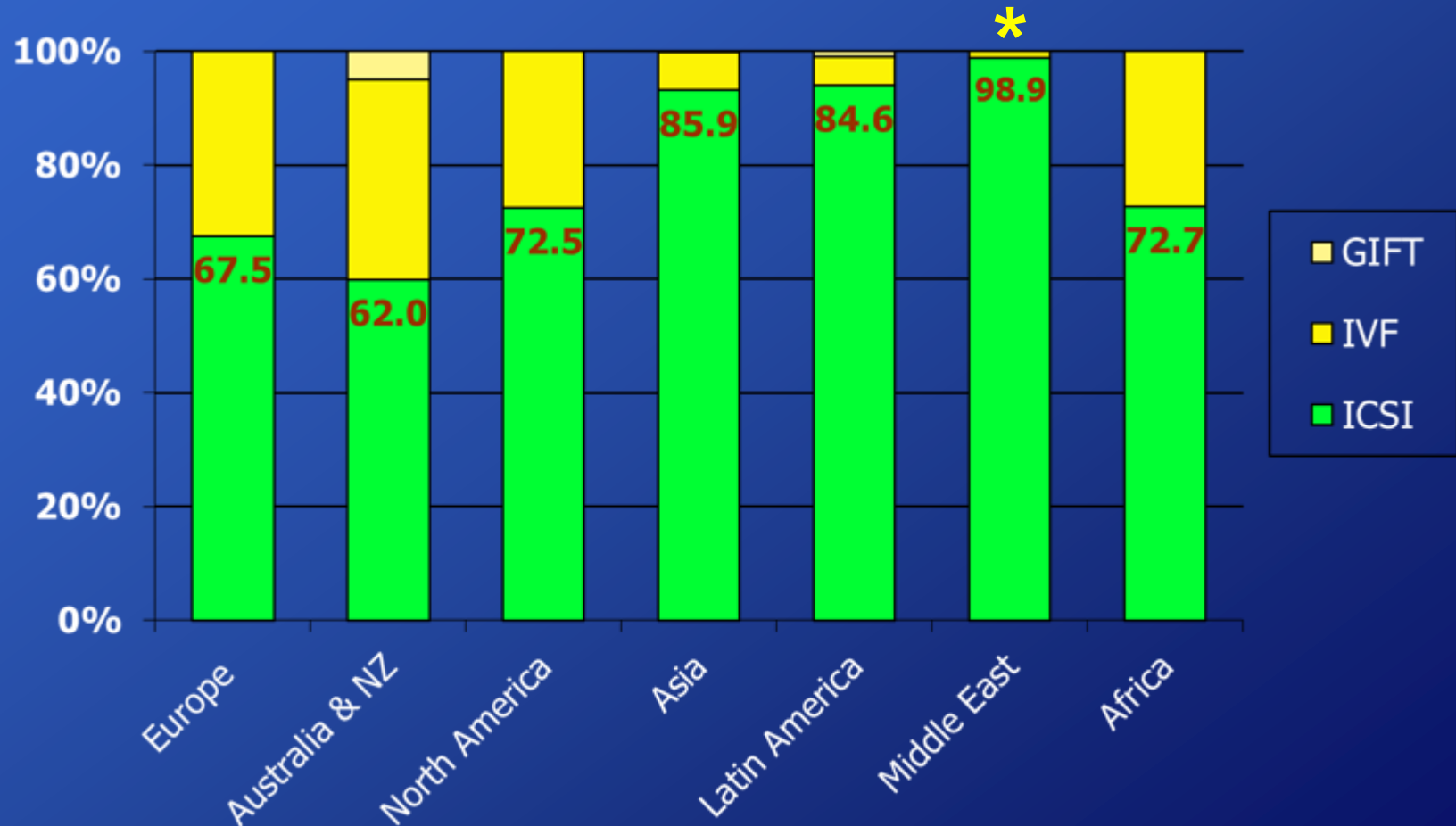
Trends in Procedure Distribution: Retrievals, FET, Egg Donation



Trends in Procedure Distribution: IVF vs. ICSI per Aspiration

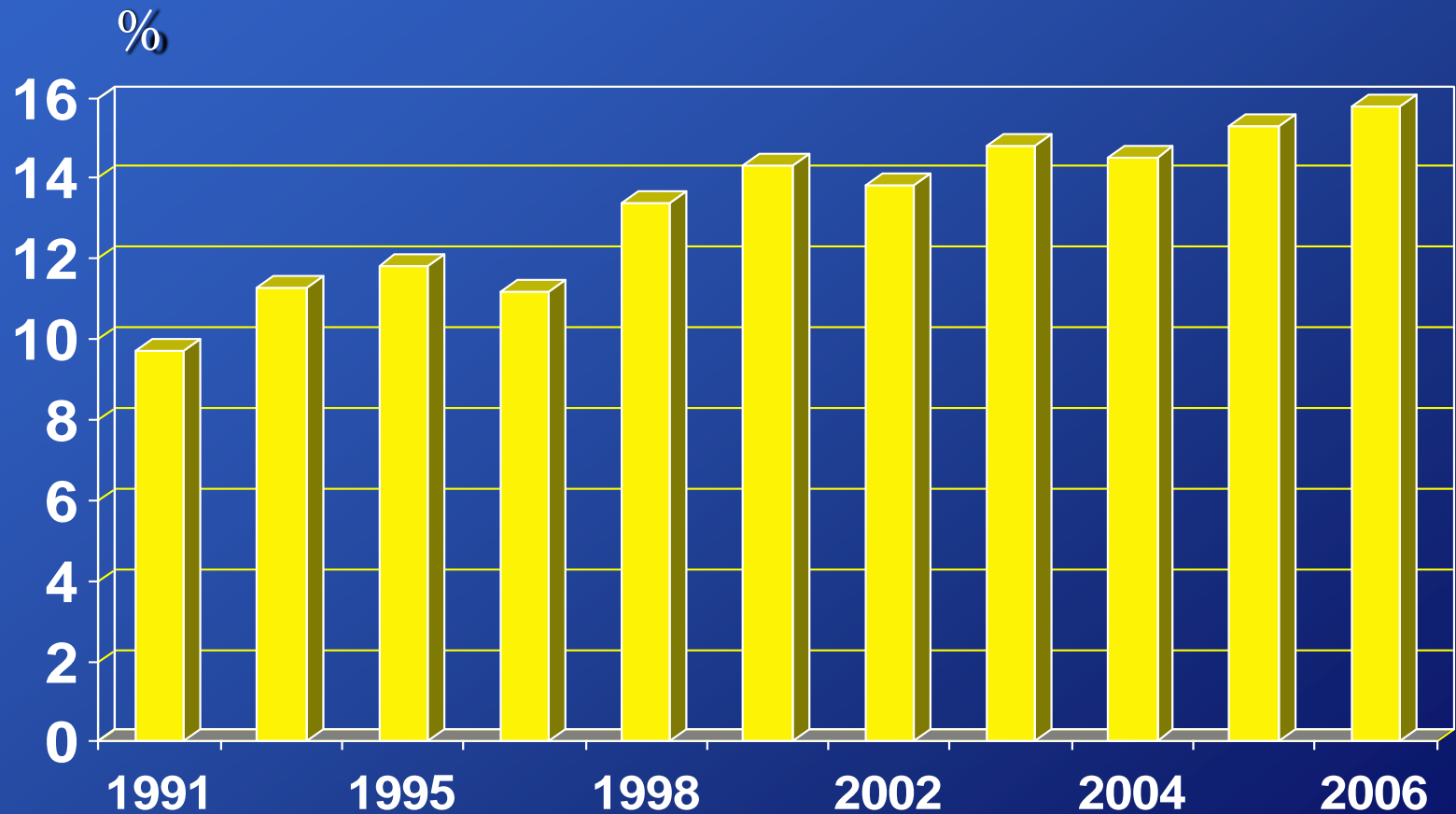


Procedure Distribution According to Region 2009

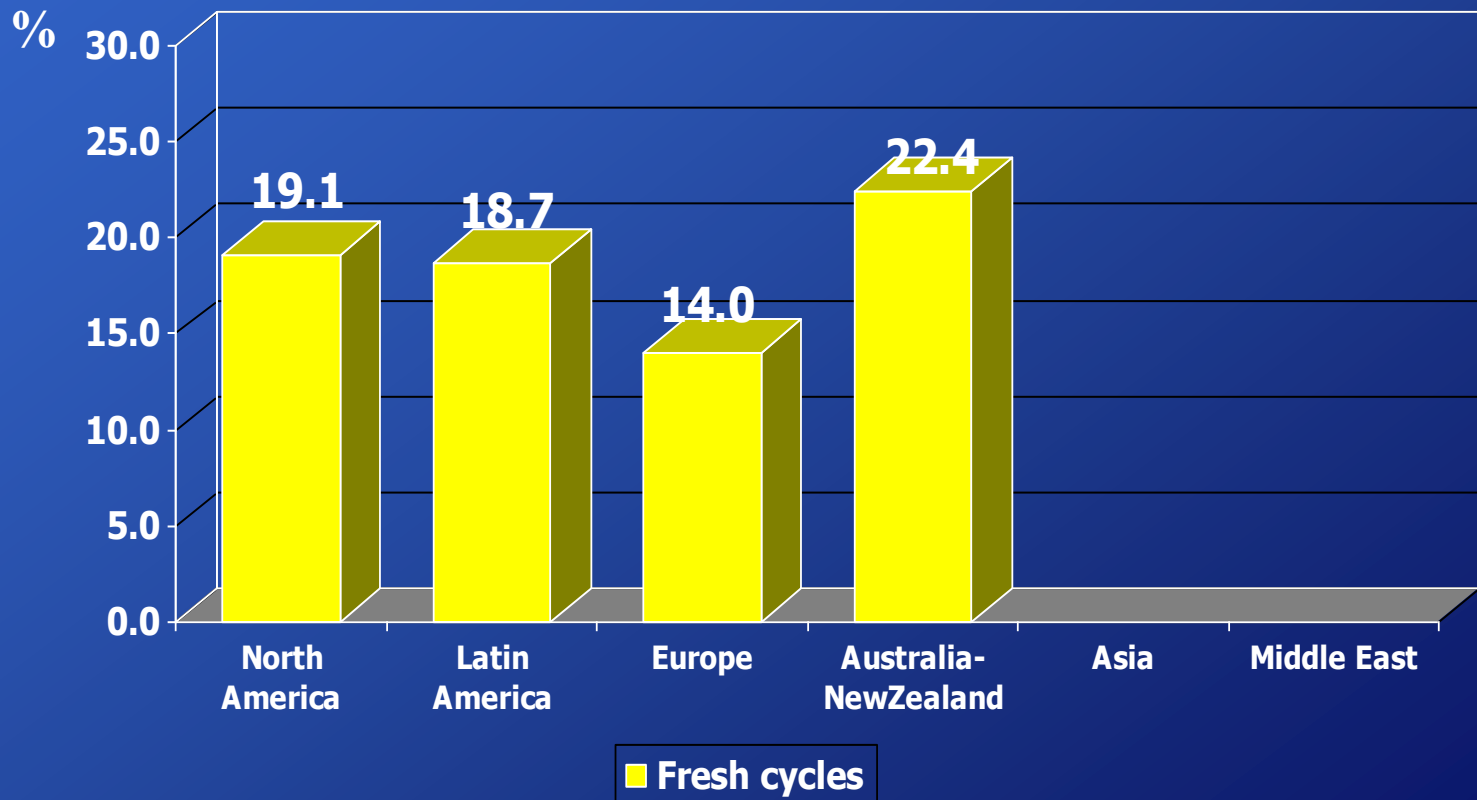


* Excluding Israel

Women's Age \geq 40 yrs



Women Age ≥ 40 By Region 2006 (IVF + ICSI)



ARS Question 2: The United States has the highest IVF pregnancy rates in the world.

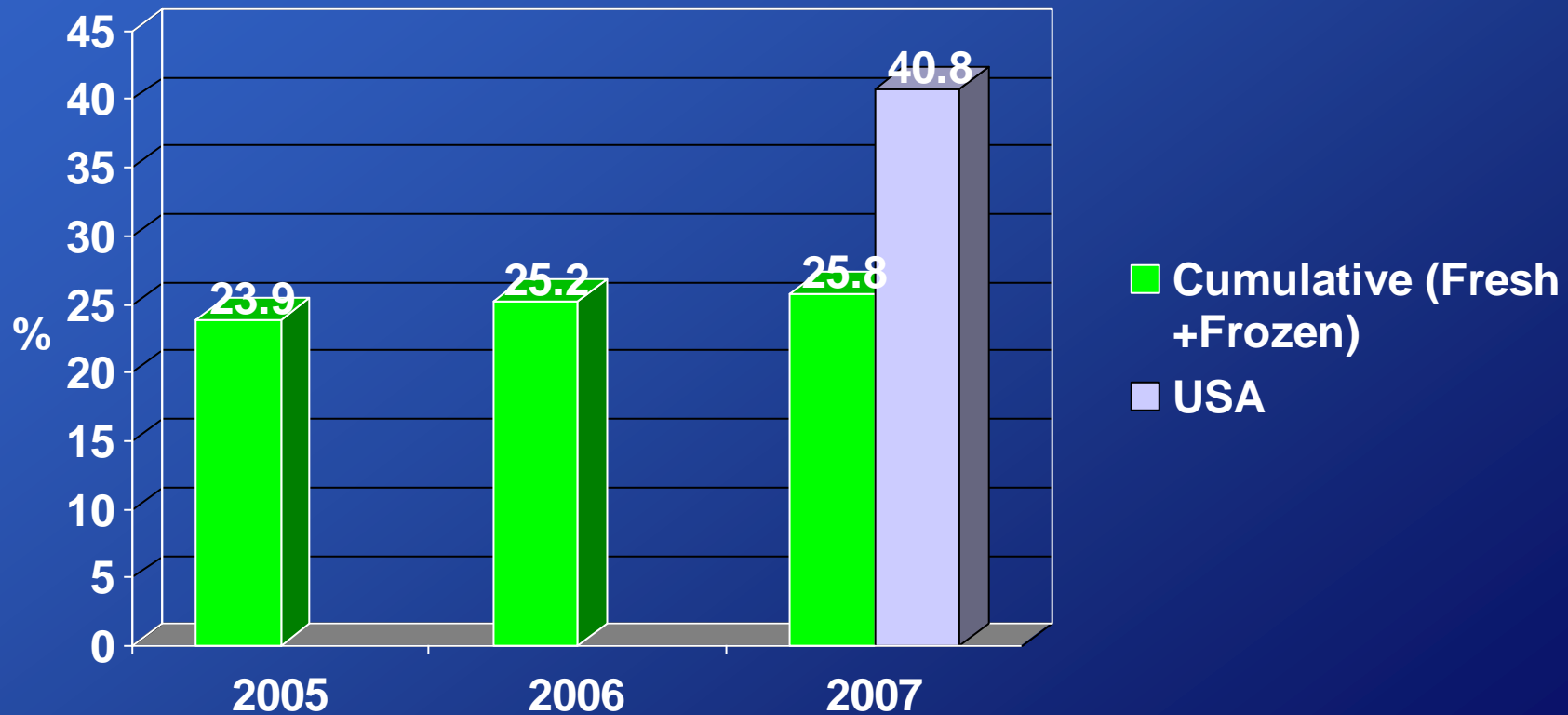
- **True**
- **False**

Effectiveness of ART



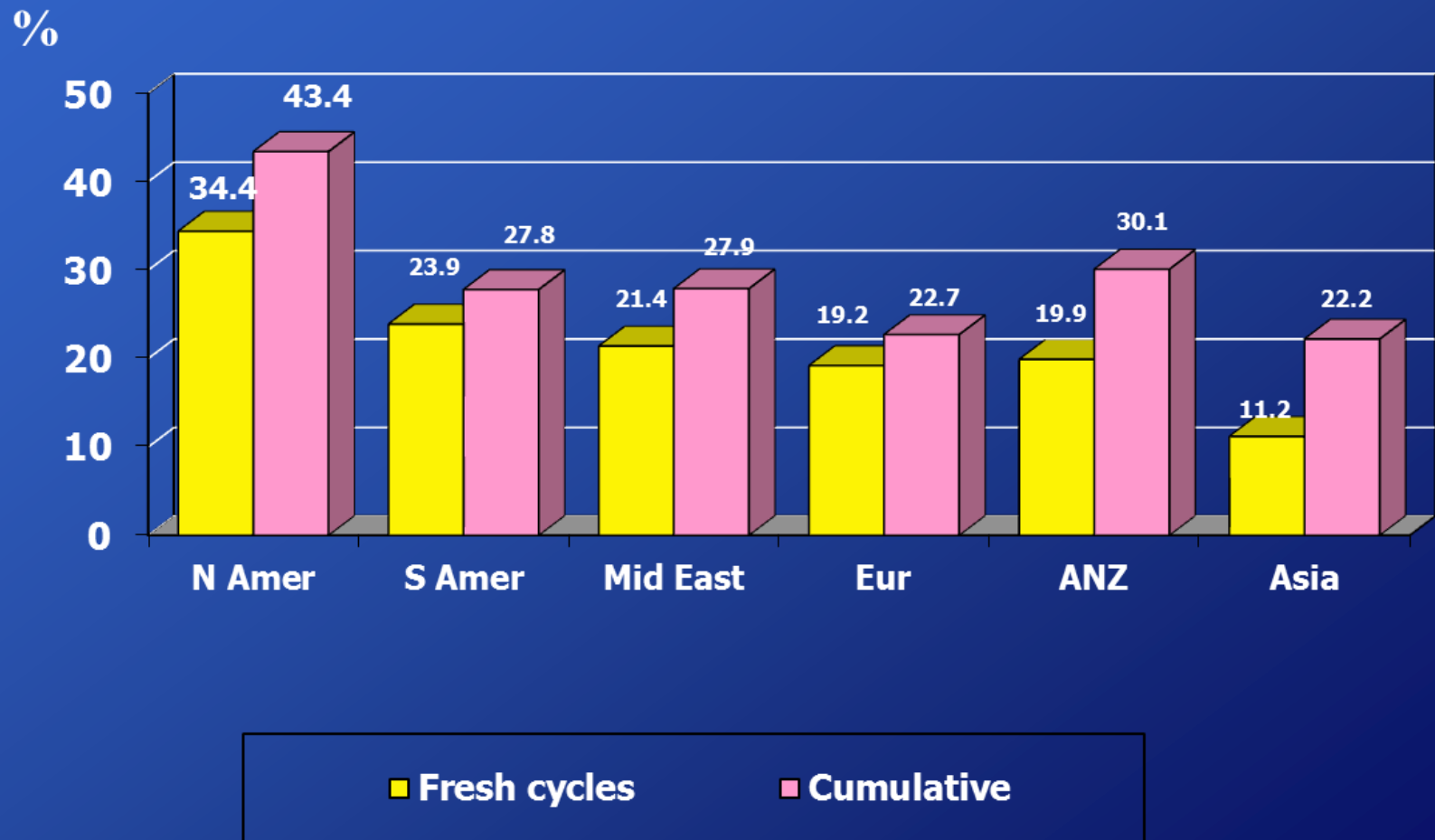
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ART 2007 Global Cumulative (Fresh + Frozen) Delivery Rate Per Retrieval



Delivery Rates per Retrieval According to Region

IVF & ICSI 2009



Numbers of Autologous ART Treatment Cycles, Procedures and Outcomes in 2003

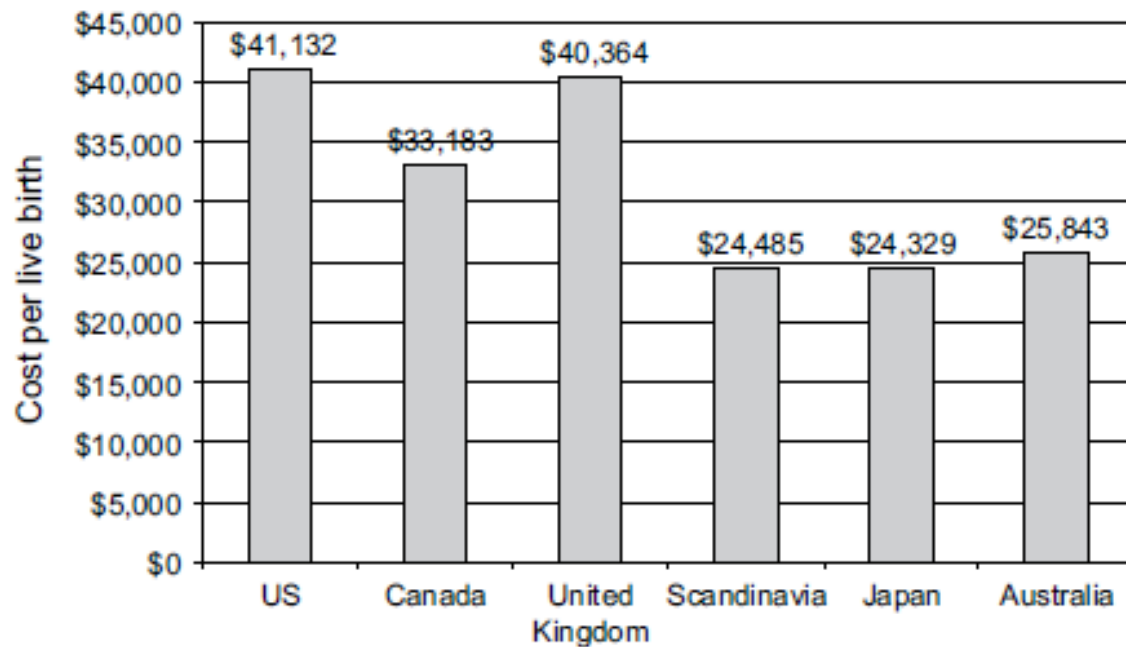
Cumulative/ Overall embryo cycles

TABLE 3						
Numbers of autologous ART treatment cycles, procedures, and outcomes in 2003.						
Variable	United States^a	Canada^b	United Kingdom^c	Scandinavia^d	Japan^e	Australia^f
Cumulative delivery rate with at least one live birth ^h (%)	37.7	31.6	28.5	26.3	20.2	28.7
Overall multiple birth delivery rate ^l (%)	32.9	30.3	24.2	17.3	16.0	17.7

Cost Per Live Birth in 2003 for Autologous ART Treatment Cycles

FIGURE 6

Cost per live birth in 2003 for autologous ART treatment cycles (USD 2006).



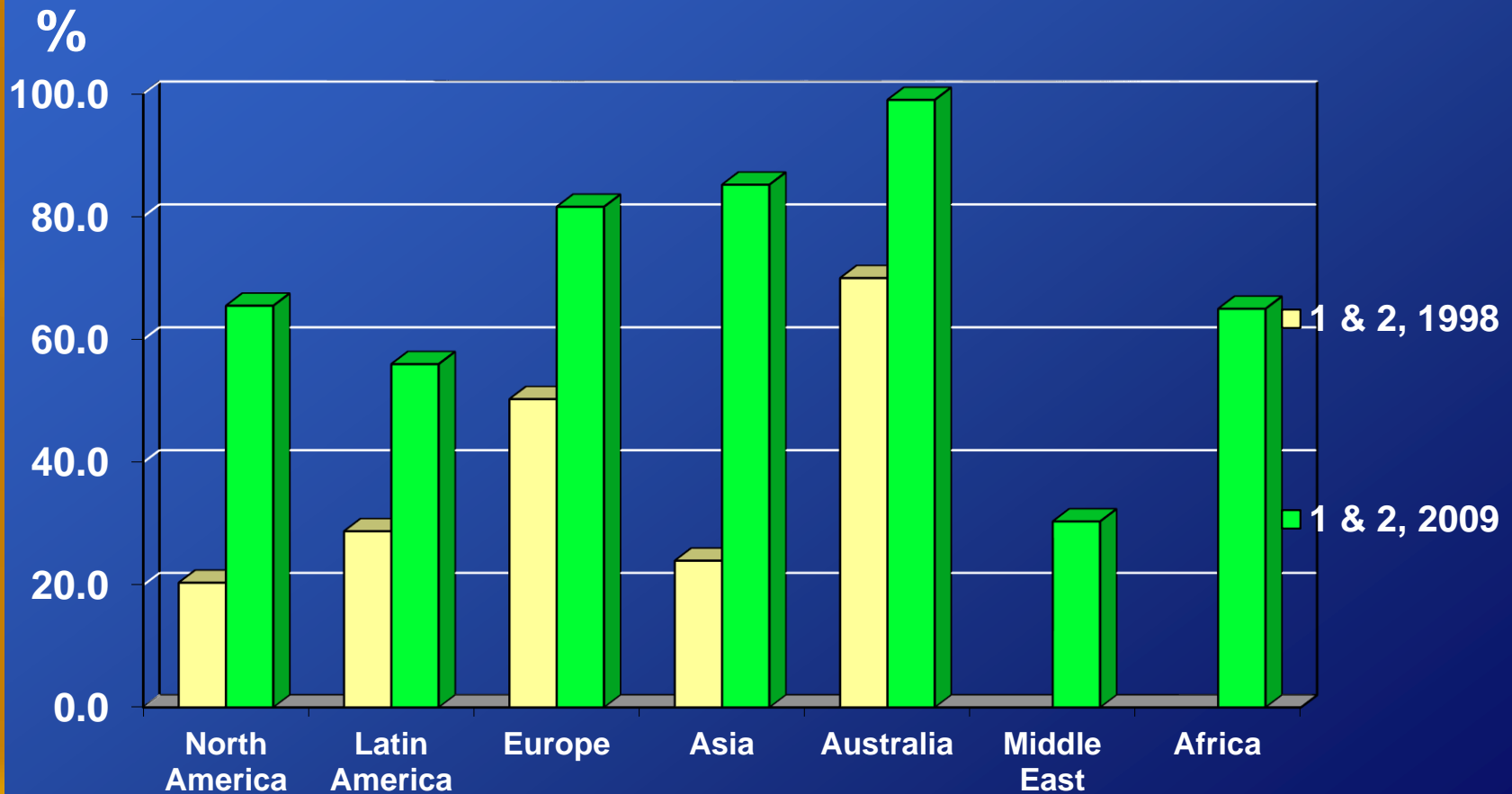
Chambers. International economic review of ART. Fertil Steril 2009.

Safety of ART

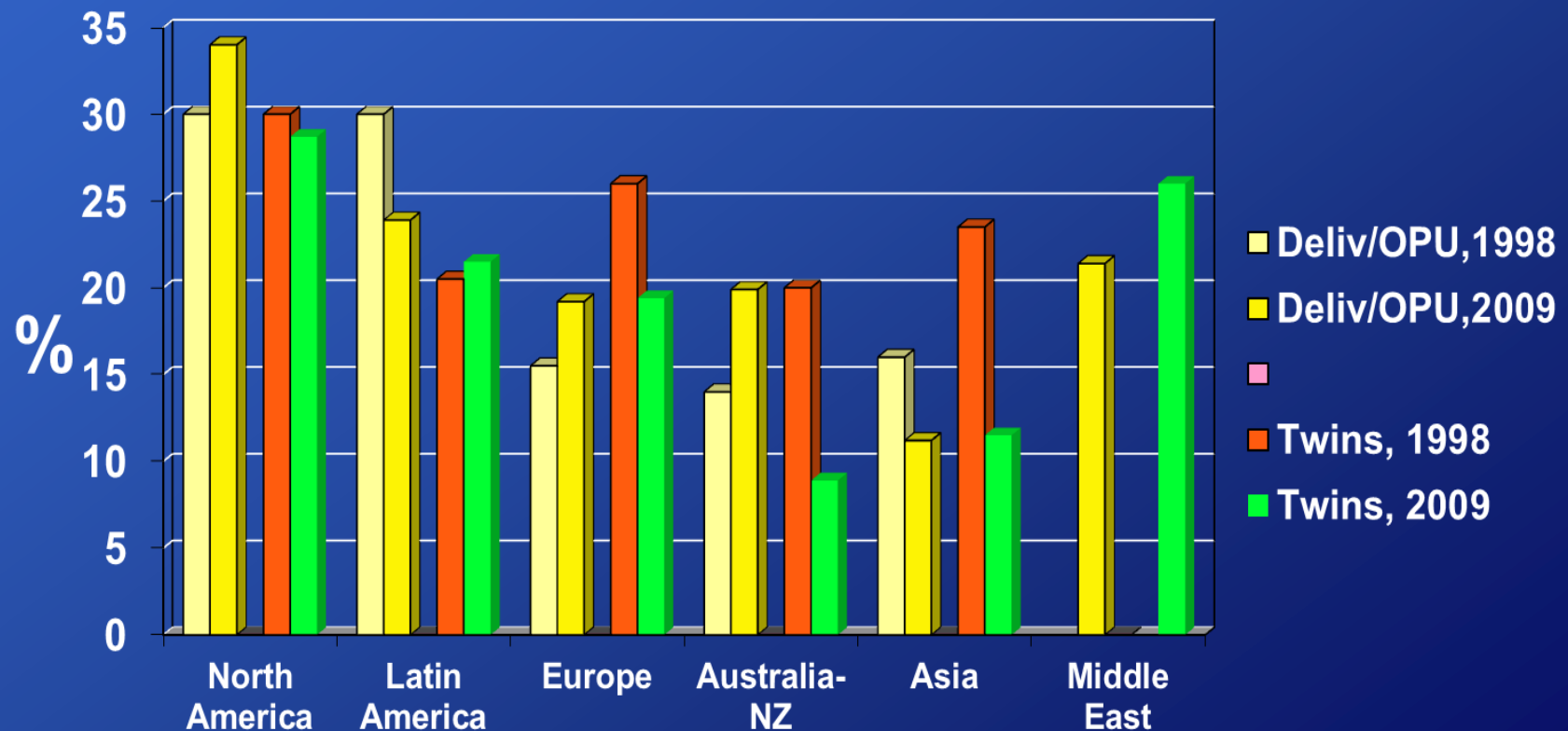


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Transfers of 1-2 Embryos per Region (%) 1998 vs. 2009

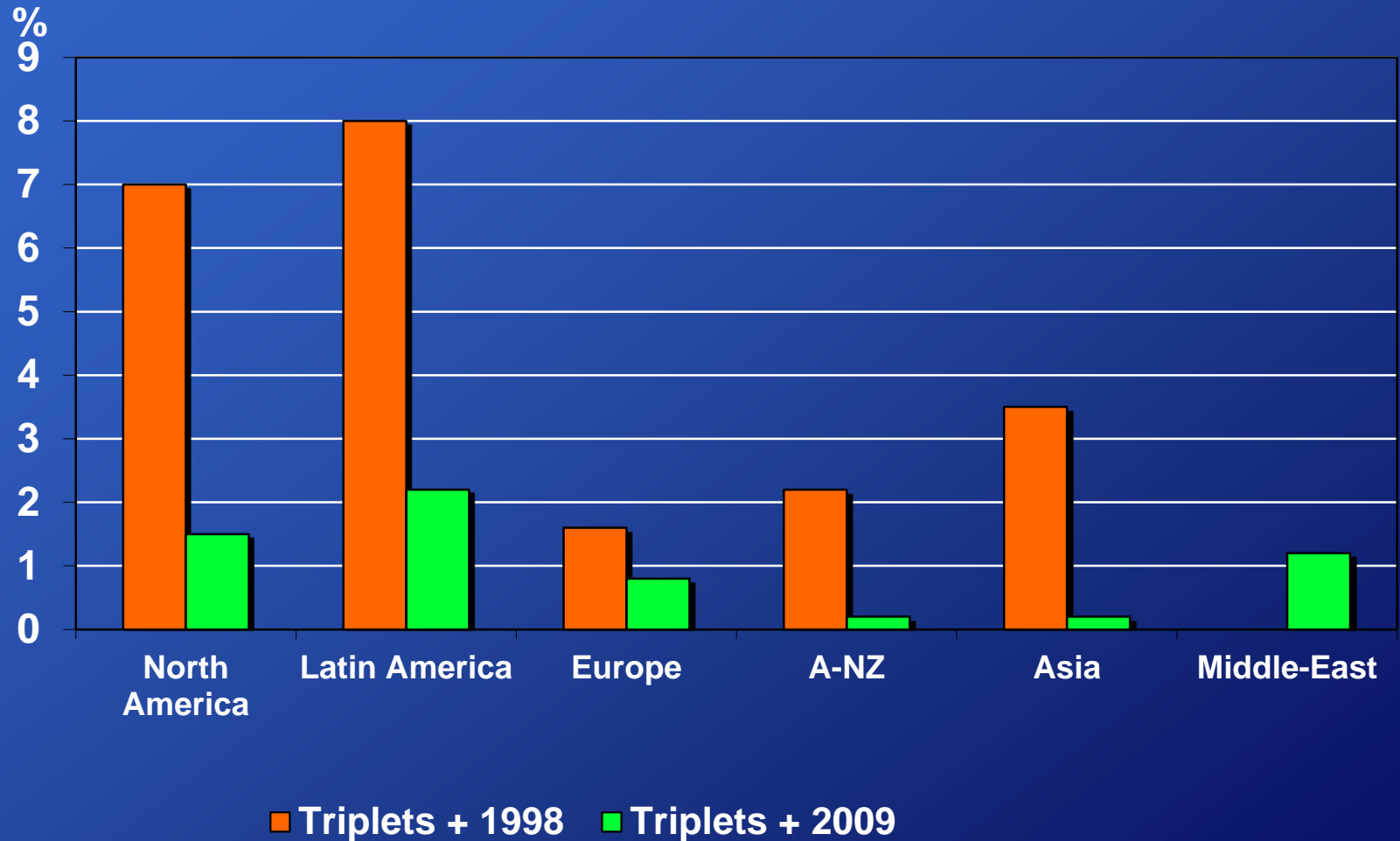


Delivery Rate (Fresh) and Twin Pregnancies per Region 1998 vs. 2009

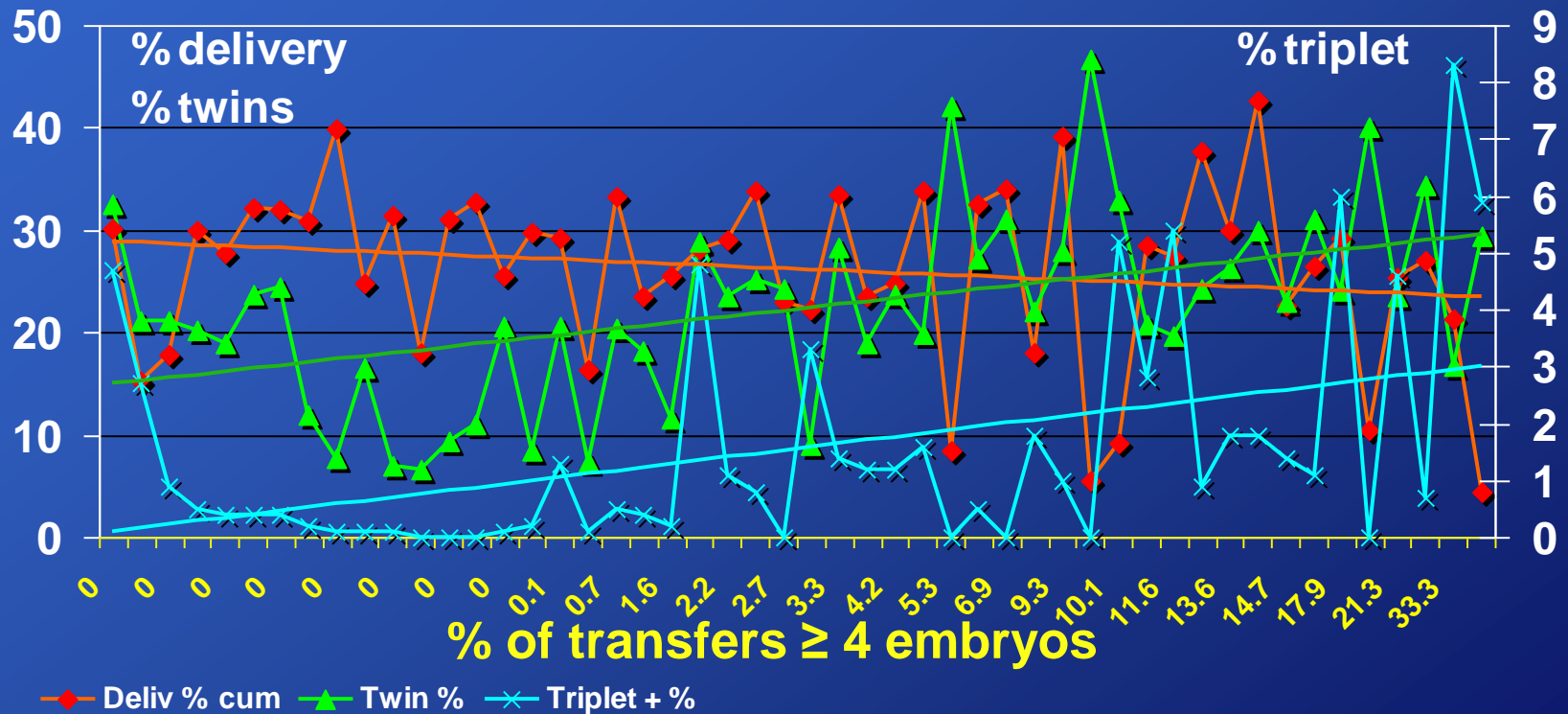


Twins 2009: 20.4%

Triplet Pregnancies per Region 1998 vs. 2009



Results and Percentage of Transfers With ≥ 4 Embryos 2008



Relation between transfers ≥ 4 and:

Delivery rate:

$r=-0.30$; $p<0.05$

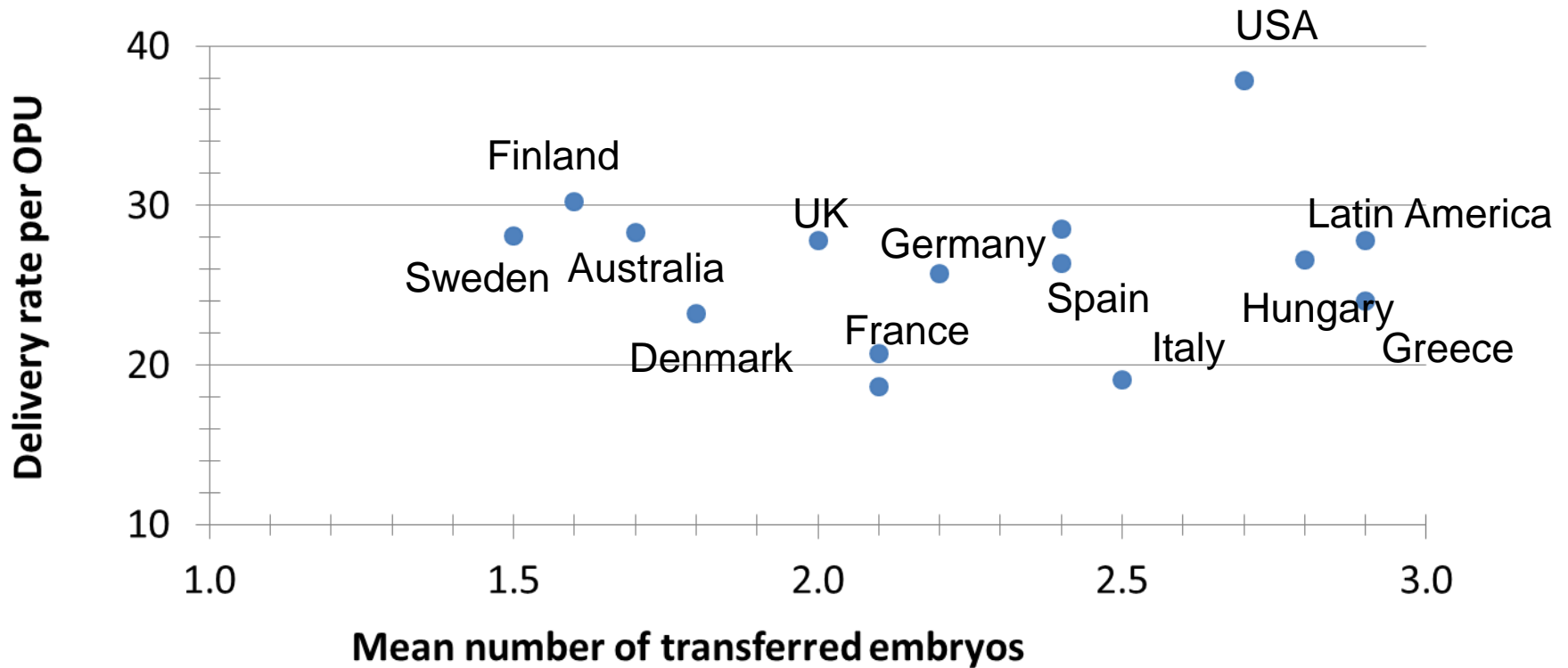
Twin rate

$r=0.41$; $p<0.01$

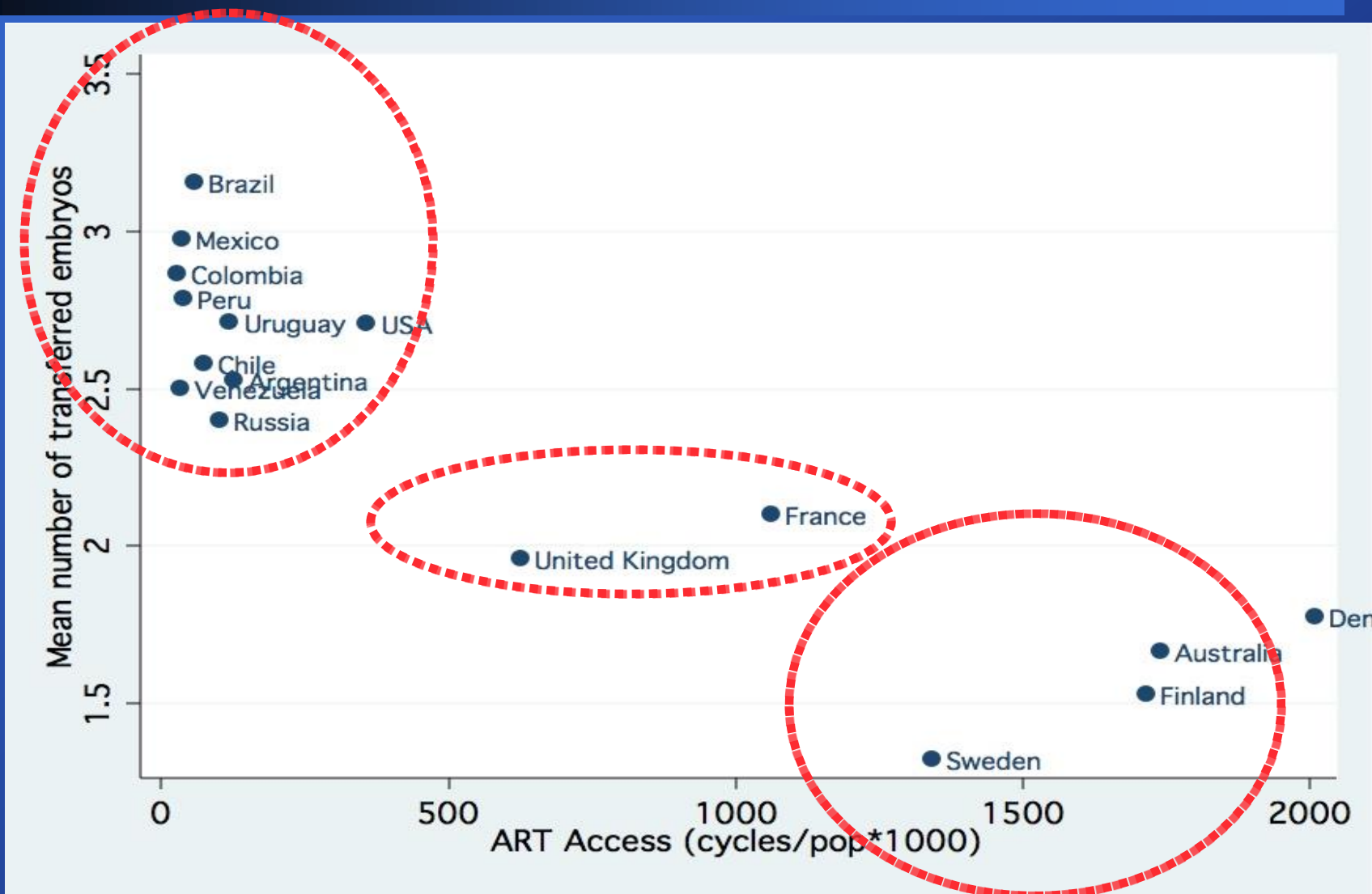
Triplet rate:

$r=0.58$; $p<0.001$

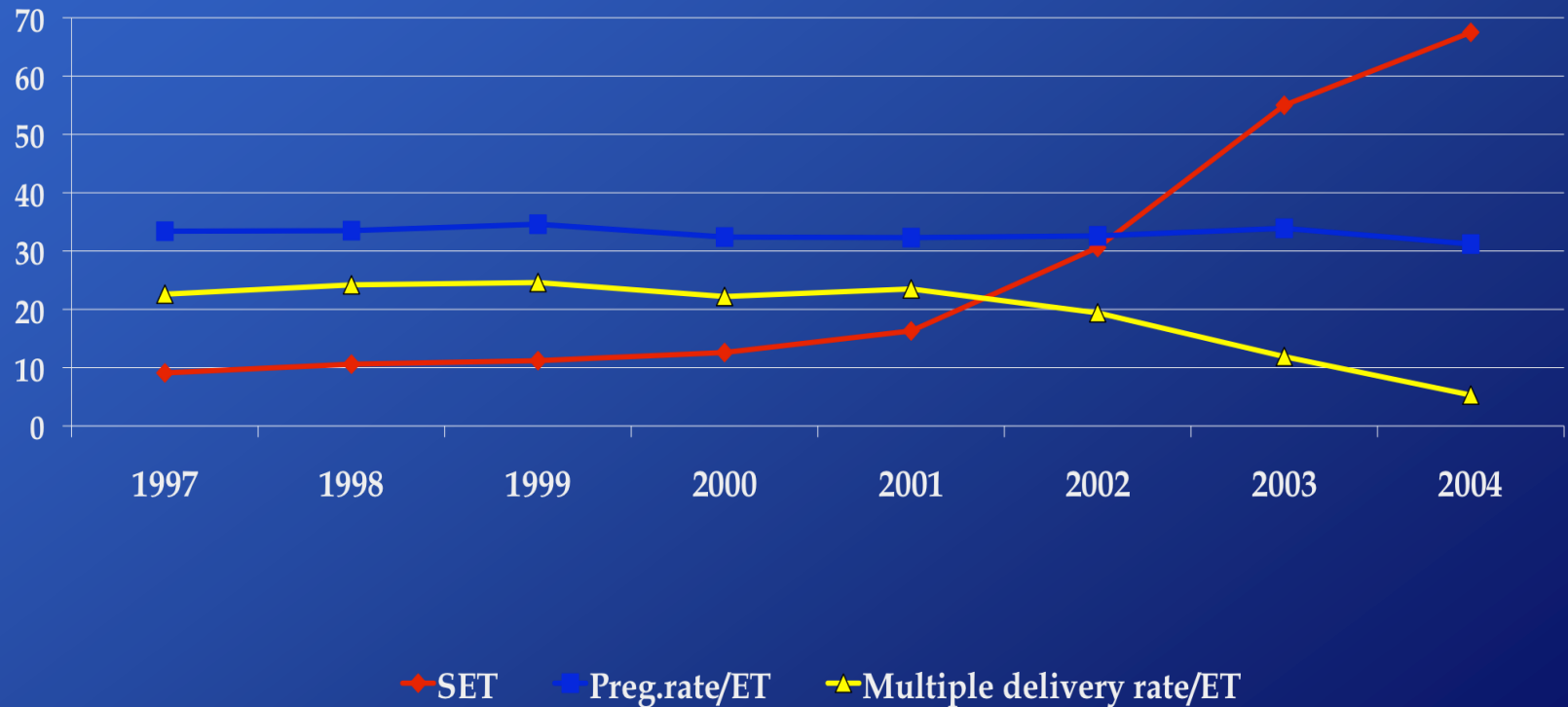
Cumulative Delivery Rate and Number of Embryos Transferred



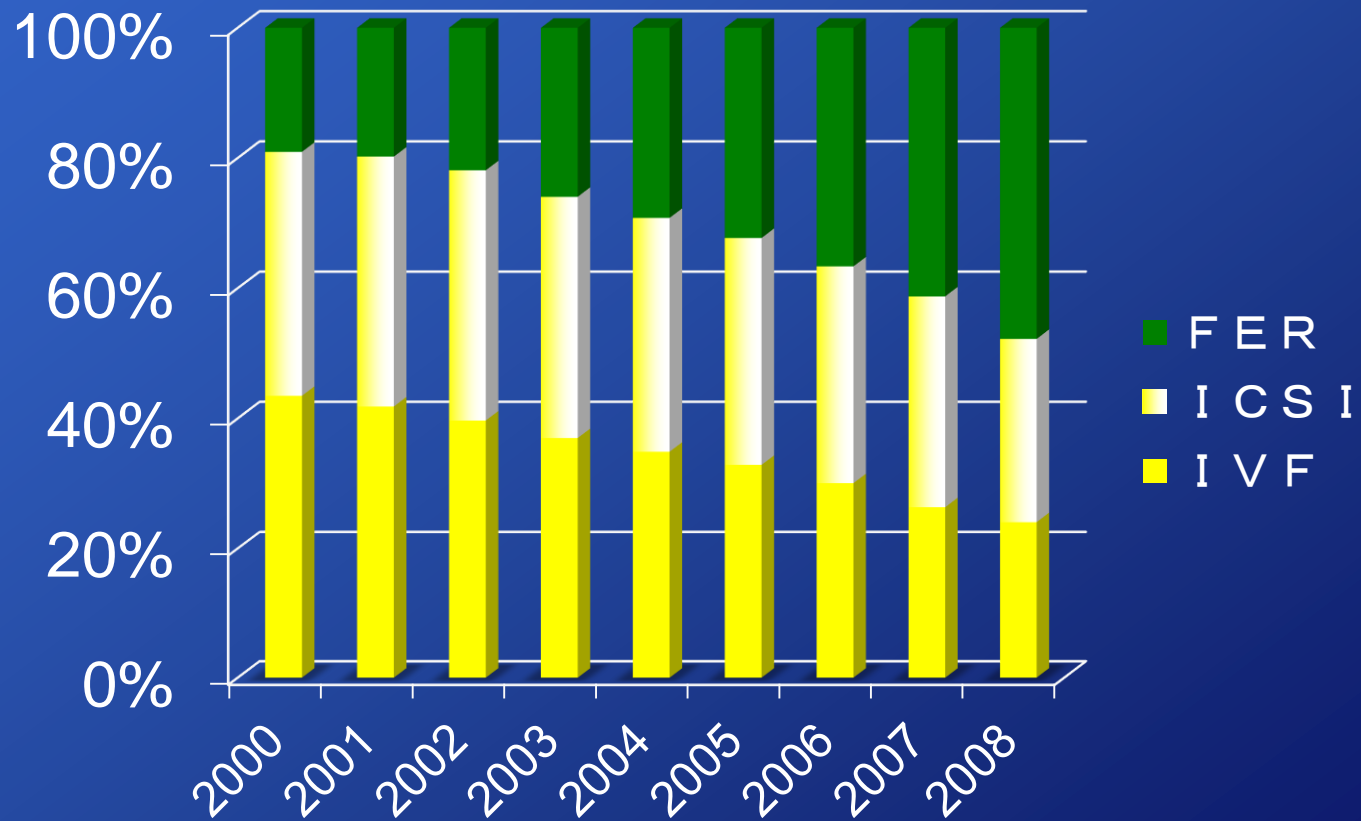
Relationship Between Access to ART And Number of Embryos Transferred



Single Embryo Transfer (SET): The Swedish Experience IVF/ICSI 1997-2004

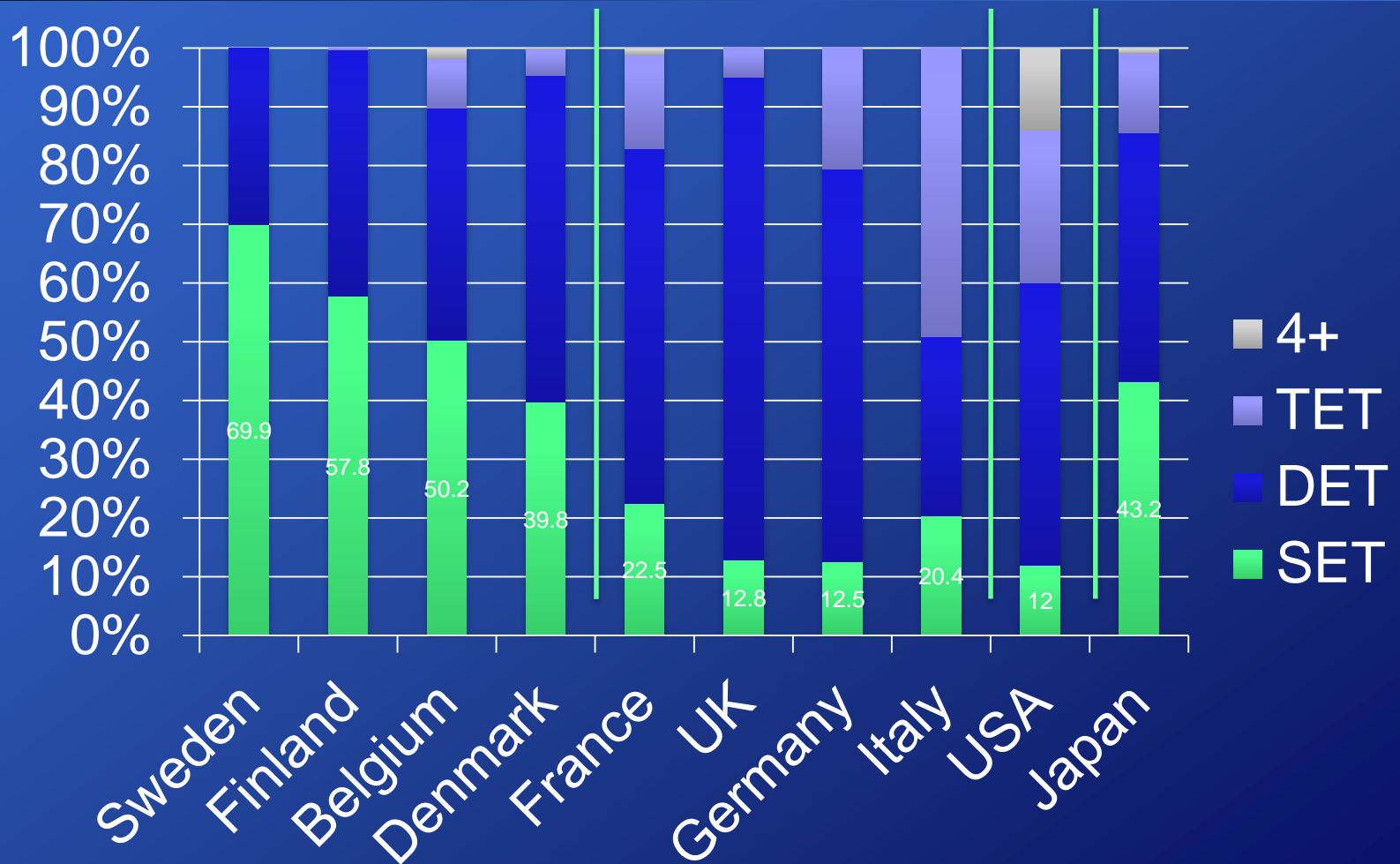


Proportion of Frozen-Thawed ET in Japan (2000-2008)



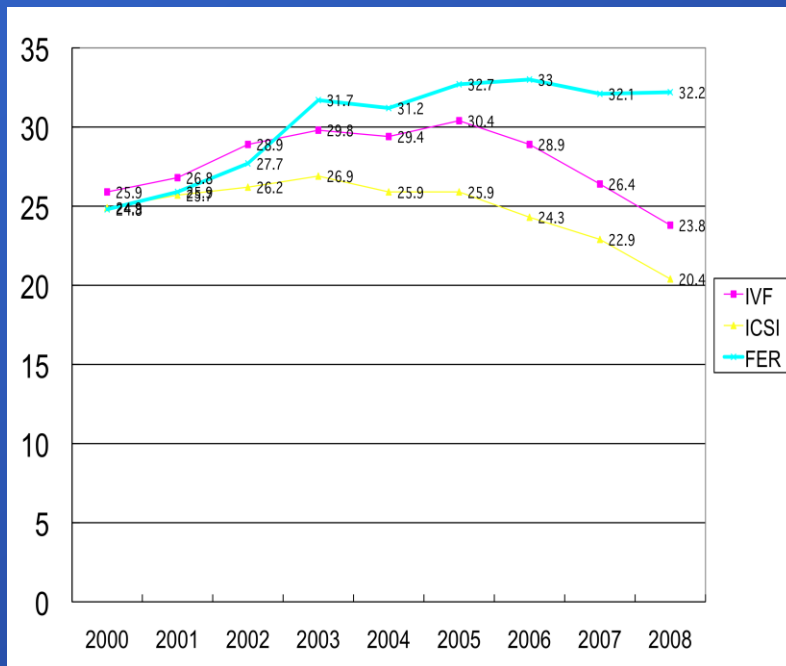
Ishihara. JSOG data

Number of Transferred Embryos (IVF&ICSI:2007)



Ishihara. ESHRE, SART and JSOG data

No Reduction of PR/ET with Frozen-Thawed ET After the Transition to SET



Clinical Pregnancy/ET

%

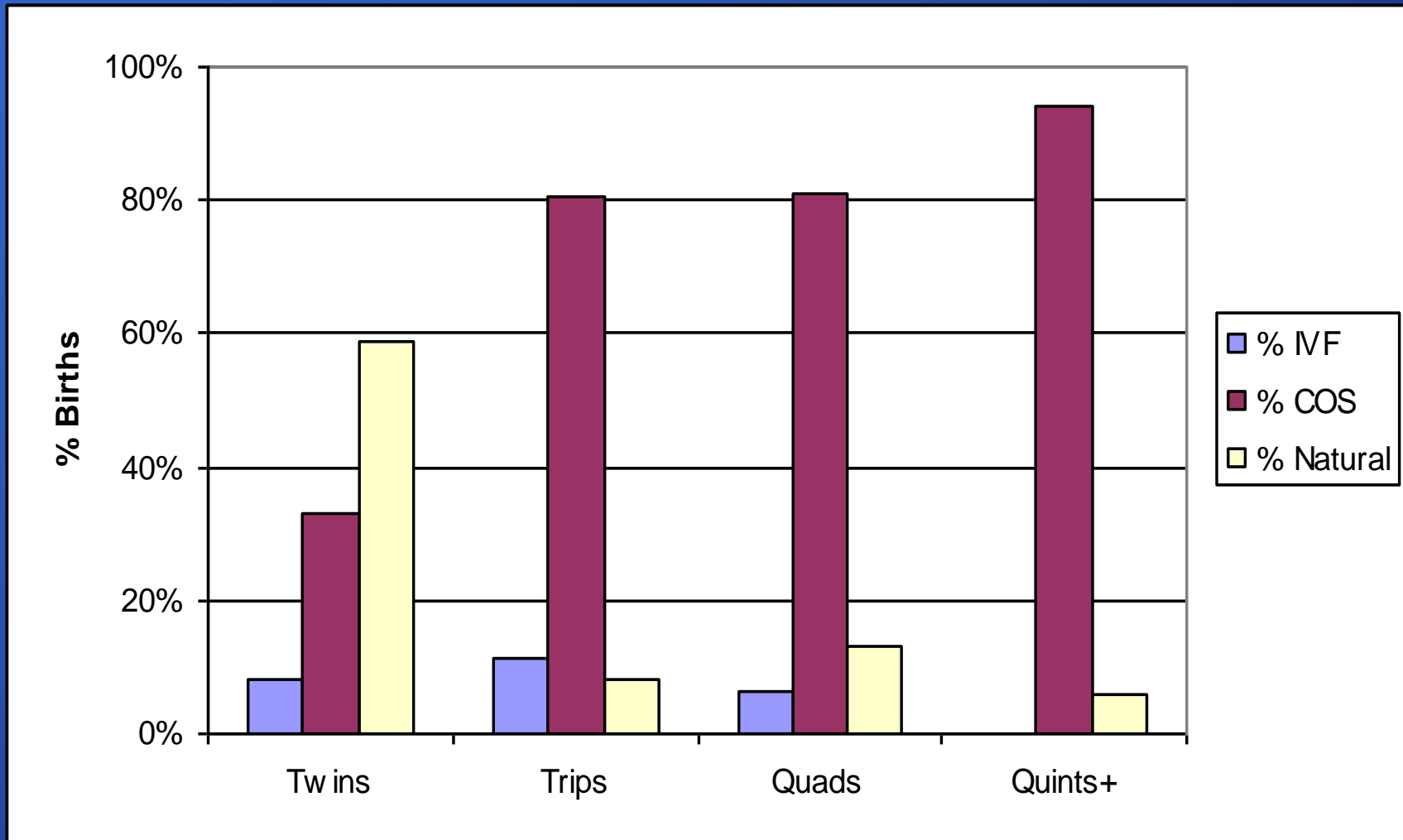


Multiple Pregnancy/Pregnancy

ARS Question 3: The biggest potential reduction in multiple births would result from fertility professionals:

1. Encouraging women to have babies at a younger age
2. Performing elective single embryo transfer on all women less than 40
3. Always limiting the number of embryos transferred to 2
4. Reducing the number of multiples resulting from controlled ovarian stimulation (COS)
5. None of the above

Multiple Births From IVF, COS, Natural United States 2006



SART. Personal Communication. 2009.

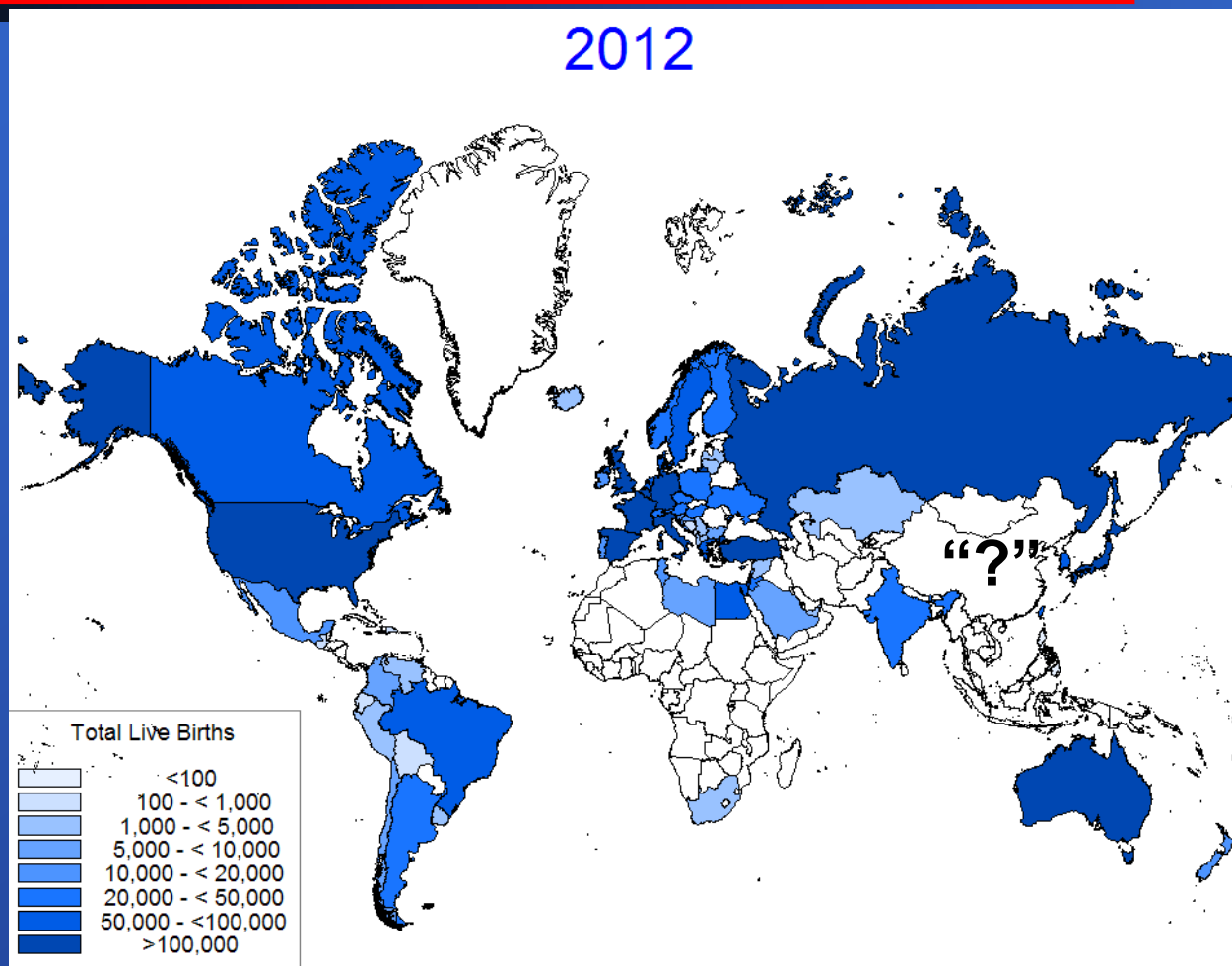
Conclusions

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Conclusions

- **1,080,479 cycles** reported (+2.0%)
 - Estimate ~1.6 million worldwide
- **243,927 babies** born (- 6,0%)
 - Estimate 400,000 Worldwide
- 67.1% ICSI (-2.0%);
- 20.3% women>40 (-0.4%)
- Mean number of transferred embryos: **1.97** (-0.11)
- **Delivery Rate** per Aspiration
 - 19.5 % (-1.3%)
 - 25.7% cumulative (+1.0%)
- **Wide differences** in availability, practice and results

Results: Global Estimated Prevalence of IVF Babies Among Reporting Countries 2012



Total Babies Born in USA and Europe

Country	Region	2012 Cumulative Live Birth Lower Boundary	2012 Cumulative Live Birth Upper Boundary
France	Europe	262,897	303,974
Germany	Europe	270,145	315,210
Spain	Europe	155,544	243,236
United Kingdom	Europe	188,724	211,215
United States	North America	642,420	799,708

Region	2012 Cumulative Live Birth Lower Boundary	2012 Cumulative Live Birth Upper Boundary
Europe	1,776,874	2,216,220
North America	696,920	863,727

Cumulative Total Number of Babies Born Globally



- Since the birth of Louise Brown on July 25, 1978, **at least 3.3 million and as many as 4.1 million babies** have been born after IVF in **countries reporting** to ICMART
- It is **likely that 1-2 million additional babies** were born during the same period in countries **not reporting** to ICMART, and in particular in China
- The number of babies born after IVF has increased rapidly in most parts of the world, with the possible exception of Africa, the Middle East and South East Asia, although this observation is potentially driven by lack of ART registration and reporting.
- **ART has established** itself as an **important technology** for fulfilling the dreams of millions of **families worldwide**



Conclusions

- **Access**
 - Much **lower than needed** worldwide
 - Even in most developed countries
- **Effectiveness**
 - **Highest in USA**, stabilized at
 - Fresh LBR/Retrieval ~ 35%
 - FET LBR/Transfer ~ 30%
 - Donor Egg LBR/Transfer ~ 55%
 - ? **Impact blastocyst and PGS**/other screening
- **Safety**
 - Much improved, BUT
 - Triplet rate needs further reduction by DET
 - **Twin rate reduction requires SET**

New ICMART Challenges



- Increase coverage
 - Geographically
 - China: Ministry of Health
 - Asia: Reps, Organizations
 - Africa: Organizations, ICMART role
 - Professional organizations
 - ICMART is an NGO with WHO
 - ASPIRE, ESHRE, ASRM
- Funding
 - Professional organizations
 - Industry
- Data Collection
 - Technology: Blastocysts/screened embryos
 - Protocols: Cryopreservation all embryos
 - Cross border reproductive care



Thank You!

International Committee Monitoring
Assisted Reproductive Technologies

The background features a light blue world map in the upper right. A large, semi-transparent globe with the acronym 'ICMART' overlaid in the center is positioned in the middle. A thick, light blue ribbon-like shape curves across the bottom right corner. Two horizontal red lines are placed above and below the 'Thank You!' text.