Prisco Piscitelli - MD PhD, Senior Epidemiologist at



Epidemiology of Osteporotic Fractures in Italy: Paradoxes

NEW UNPUBLISHED DATA

Aknowledgements: Prof. UMBERTO TARANTINO

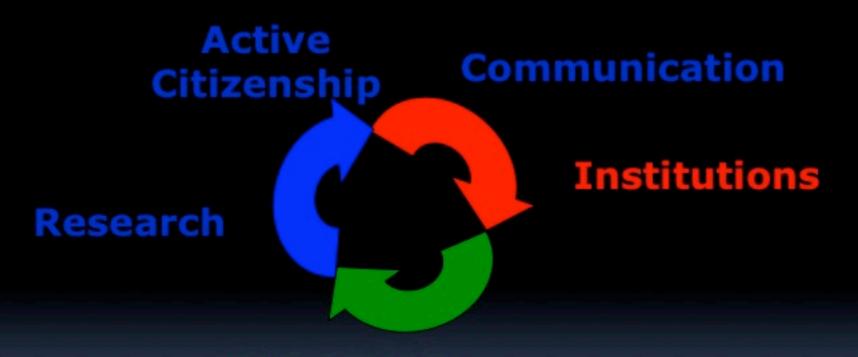
ISBEM e la sua anima...



«Monastry of Third Millenium» Project



ISBEM VISION



ISBEM TALENT HUB

60 PhD additional positions from 1999 and 2017

 Inclusion of young post-graduate in Research Groups

ISBEM RESEARCH TOPICS

Osteoporosis and Fractures (EMEROS = 10.000 patients)

Cardiovascular

Environmental Epidemiology and Oncology

Statistics Clinical Trial CRO



EUROPEAN INNOVATION PARTNERSHIP

on Active and Healthy Ageing

European Commission > EIP on AHA > Repository of practices > EURO MEDITERRANEAN REGISTRY OF OSTEOPOROSIS



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EURO MEDITERRANEAN REGISTRY OF OSTEOPOROSIS

the Euro Mediterranean Bio-Medical Scientific Institute (ISBEM, Brindisi, Italy) has launched a pilot project for the disease management of osteoporosis, which is aimed at the prevention of fragility fractures through the early identification of people at higher risk through the use of phalangeal QUS and the collection of clinical risk factors in the R.O.I.S. registry (Ionian and Salento Osteoporosis Registry) which represents the first section of the EMEROS (Euro Mediterranean Registry of Osteoporosis), acknowledged as official commitment by the European Commission Action Group on Active and Health Ageing. The registry has started in 2009 thanks to a strong cooperation between ISBEM researchers and physicians from the Local Health Authorities ASL Brindisi, ASL Taranto and ASL Lecce (limited to the hospital of Gallipoli, Division of Orthopedics and Traumatology). This first section of the registry is of particular interest because Salento sub-region represents the "oldest" area of Apulia and Italy.

DETAILS

15/09/2016

Acronym: EMEROS

Initiative status:

On-going

Initiative URL: http://www.isbem.it

Total budget: €100.00 - €499,999

Contact person: PRISCO PISCITELLI

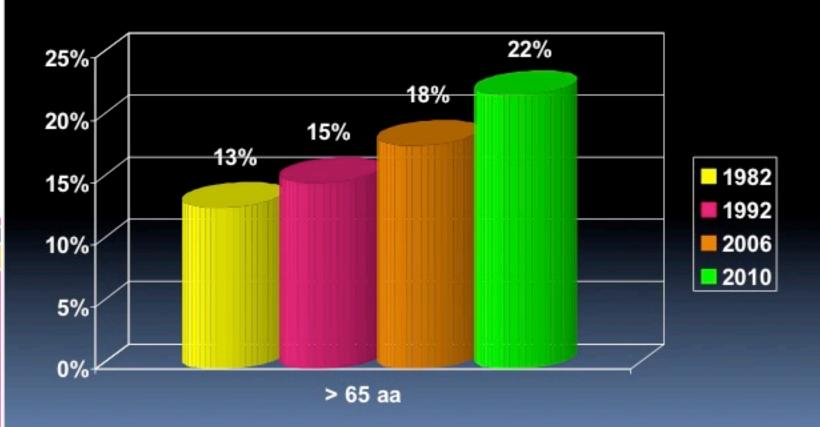
The Epidemiological Paradox



- Life Expectancy at birth has rised at about 4 months per year from 1950:
- 76.2 ♂ & 86.6 ♀ in 2000
- 77.9 ♂ & 87.4 早 in 2010

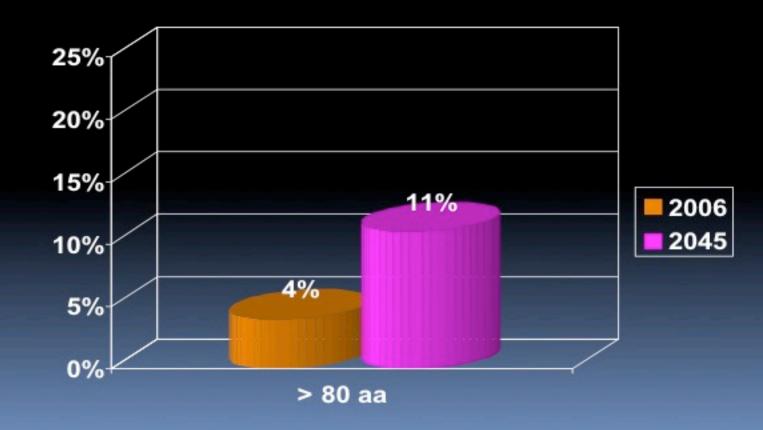
The Third Age of the life

More than 20% of the Italian population is > 65 years old: 10 million people or 1 woman out 5 & 1 man out 7.



The «Fourth» Age of the life

- The 4% of Italian population is >80 years old.
- They will be 11% within 30 years



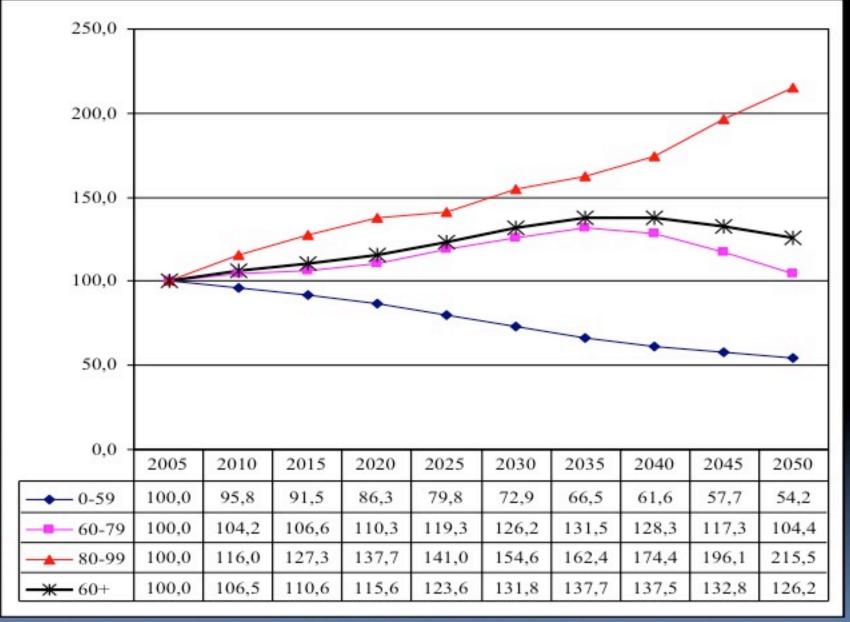
A «fifth» Age of the life?

Although 70% of total deaths in Italy occurr between 70 and 90 years old, up to 3,5% of deaths is currently recorded at 90 years of age and older: a fifth age?

The age of disability?



The Ageing of Italian Population



Osteoporosis in Italy

- Abut 5 million people are estimated to suffer from osteoporosis in Italy but in the majority of cases a specific diagnosis has not been made.
- Giving the ageing of the Italian population, the prevalence of osteoporosis will increase progressively.

Osteoporosis per age groups

L L		9 - 9 - 1 - 1 - 1
Classi di età DONNE	Osteoporosi	
40-49	363.400	
50-59	581.000	
60-69	1.093.000	
70-79	1.260.300	
80-100	1.311.700	
Totale donne	4.609.000	
	Classi di età UOMINI	Osteoporosi
	60-70	386.350
	70-80	340.750
	80-100	256.080

Totale uomini

983.180

The Fragility Fracture Paradox

Hip Fractures Incidence in Italy: Methodology of our work

- The first study in Europe to assess the incidence of hip fractures by using national hospitalization records;
- The first study to compare the economic burden of hip fractures to that of acute myocardial infarctions;
- Osteoporos Int. 2007 Feb;18(2):211-9.
- ICD-9CM codes of diagnosis considered for hip fractures:
- 820.0 e 820.1 (femoral neck),
- 820.2 e 820.3 (intertrocanteric fractures),
- 820.8, 820.9 e 821.1 (other femoral fractures).

Rationale

- Our intention is to perform a comparison analysis between hip fractures of the elderly and two different pathologies whose severity is well appreciated by healthcare operators and the public. As comparators, we chose acute myocardial infarction (AMI) and strokes.
- Like hip fractures, both strokes and AMI have multiple risk factors and a high prevalence among the general population; moreover, they are expected to produce high healthcare costs, and preventive measures represent a critical issue as for hip fractures.

Hip Fractures in Italy

NEW UNPUBLISHED DATA - Piscitelli & Tarantino - Under Submission to OP Int

More than 1 Million Hip Fractures in people > 65 y.o. (1.140.401) from 2000 to 2014.

- 2010: 21820 M + 70729 F = Total 92.549
- 2011: 21950 M + 69783 F = Total 91.733
- 2012: 22222 M + 71186 F = Total 93.408
- 2013: 22299 M + 71817 F = Total 94.116
- 2014: 22643 M + 71882 F = Total 94.525
 +3.7% M 2014 VS 2010 + 1.6% F 2014 VS 2010 Tot + 2.1% 2014 VS 2010

Hip Fractures in Italy

- About 400.000 deaths after hip fracture event and more than 200.000 cases of total disability.
- Direct costs for the National Healthcare System sustained from year 2000 to 2014: 13,5 Billion Euros including rehabilitation costs.
- Estimated 1,5 Billion Euros paid for social aid to disabled people.

YEAR (Italy)	COSTS (MILLION EUROS)	
2007	911,555,558	
2008	941,374,079	
2009	947,854,597	
2010	941,547,028	
2011	933,245,454	
2012	950,286,063	
2013	957,488,899	
2014	961,649,860	

REGION	Overall Costs 2007 (€)	Overall Costs 2014 (€)	
Valle D'Aosta	2.404.342	3.490.173	
Piemonte	136.116.764	147.517.998	
Lombardia	200.134.302	231.033.970	
Trentino A. A.	25.051.690	26.168.544	
Veneto	89.162.298	95.491.145	
Friuli V. G.	32.823.142	29.751.789	
Liguria	50.134.402	52.104.411	
Emilia Romagna	a Romagna 109.219.162 116.370.139		

REGIONE	Overall Costs 2007 (€)	Overall Costs 2014 (€)	
Toscana	101.525.268	103.976.145	
Umbria	25.548.070	28.309.185	
Marche	40.408.452	43.603.901	
Lazio	164.441.461	131.028.867	
Abruzzo	32.326.762	36.856.231	
Sardegna	31.799.358	33.939.998	

REGIONE	Overall Costs 2007 (€)	Overall Costs 2014 (€)
Campania	94.482.873	108.459.079
Molise	8.857.284	9.089.963
Puglia	80.460.132	88.867.572
Basilicata	15.527.394	16.768.345
Calabria	38.841.753	47.373.288
Sicilia	110.615.230	116.059.901

Hip Fractures vs. AMI and Strokes Direct Costs

	YEAR	People aged >65 HIP FRACTURES	Total adults >45 AMI	People aged >65 AMI	Total adults >45 STROKE	Total adults >45 TIA
-		DIRECT COSTS MILLION EUROS Including Rehabil.	DIRECT COSTS MILLION EUROS Including Rehabil	Direct Costs Including Rehabiltiation	Direct Costs Excluding Rehabiltaion	Direct Costs Excluding Rehabiltaion
	2001	890	654	428	574	149
_	2002	924	691	472	589	147
	2003	999	729	507	573	138
	2004	1.043	747	518	570	135
	2005	1.090	794	568	560	129
		,	Piscitelli. Iolascon	et al. Clin Inte	ervention in Agi	na 2012

MORTALITY

Hip Fractures

- Acute 1-month Mortality: 5-15%
- 1 Year Mortality: 15-30%

AMI:

- Acute 1-month Mortality: 15-25%
- Mortalità ad 1 anno: 15-18%

Stroke:

- Acute 1-month Mortality: 17-34%
- 1 Year Mortality: 10-15%

More about Hip Fractures in Italy

- About 67,5% of all hip fractures occurring in elderly people are suffered >80 years old!
- About 40% of all hip fractures occurr in Women >85 (which represent only 4.4% of the Italian population)!
- And 16,5% of hip fractures are experienced by people >90 years old (which represent only 1.1% of the Italian population)!

>85 Years Old = HIGHER RISK OF FRACTURE!

More about Hip Fractured elderly people of 2014 (Total: 94.525)

- 44.471 hip fractures occurred in people >85 years old (34.636 women & 9.835 men)
- 23.242 hip fractures in people 80 84 years old (17.720 women & 5.522 men)
- 14.544 hip fractures in people 75 79 years old
 (10.808 women & 3.736 men)
- 7.887 hip fractures in people 70 74 years old
 (5.682 women & 2.205 men)
- 4.381 hip fractures in people 65 69 years old
 (3.036 women & 1.345 men)

Even more details (Year 2014)

- 67.713 hip fractures >80 years old (F:2.6% & M: 1.3%) (52.356 women & 15.357 men)
- 15.524 hip fractures >90 years old (F:3.7% & M: 8.3%) (12.574 women & 2.950 men)
- Over 80 years old we have 67.713 new hip fractures That is 71.6% of the total 94.525 occurring in people aged >65 but 16.4% occurred > 90 y.o.

The SIOT Axiom

Hip fractures in the elderly (in our case: very elderly)

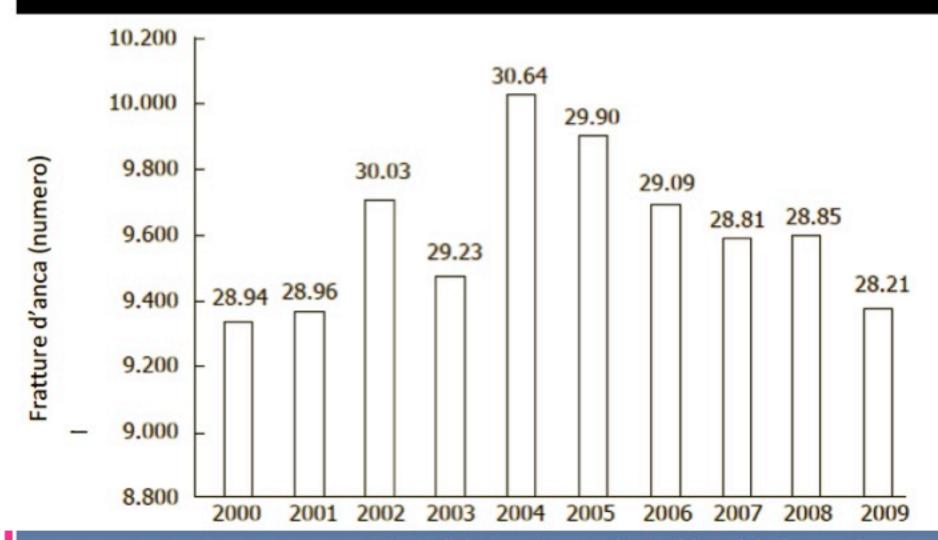
SURELY (No Doubts) FRAGILITY FRACTURES

The Paradox of temporal trends

- Hip Fractures occurred in people >65 years olds INCREASED by a +22% from 2000 to 2014 (from 73493 in year 2000 up to 94525 in 2014):
- + 20% in women
- + 28% in men

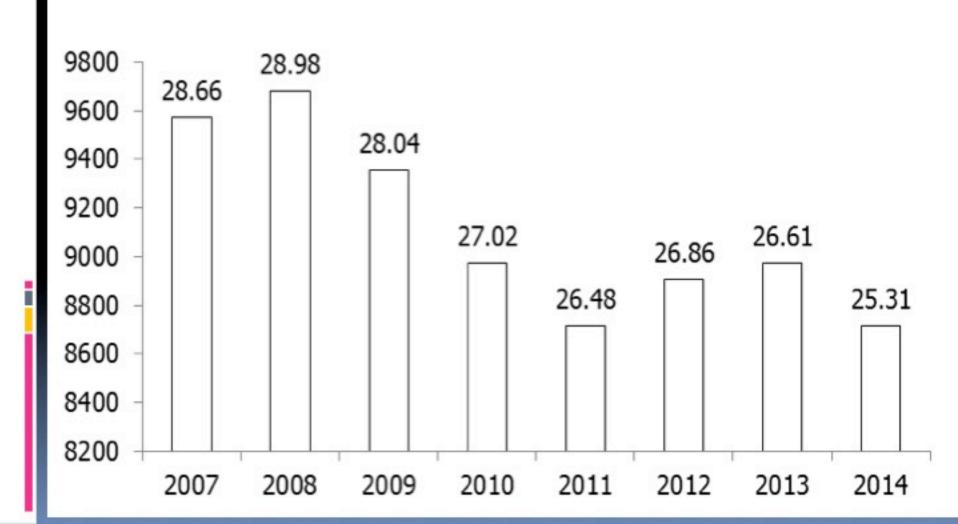
BUT....

For the First time in Italy a decreasing trend in women 65-74



The trend is still decreasing

NEW UNPUBLISHED DATA - Piscitelli & Tarantino - Under Submission to OP Int



The case history of this study



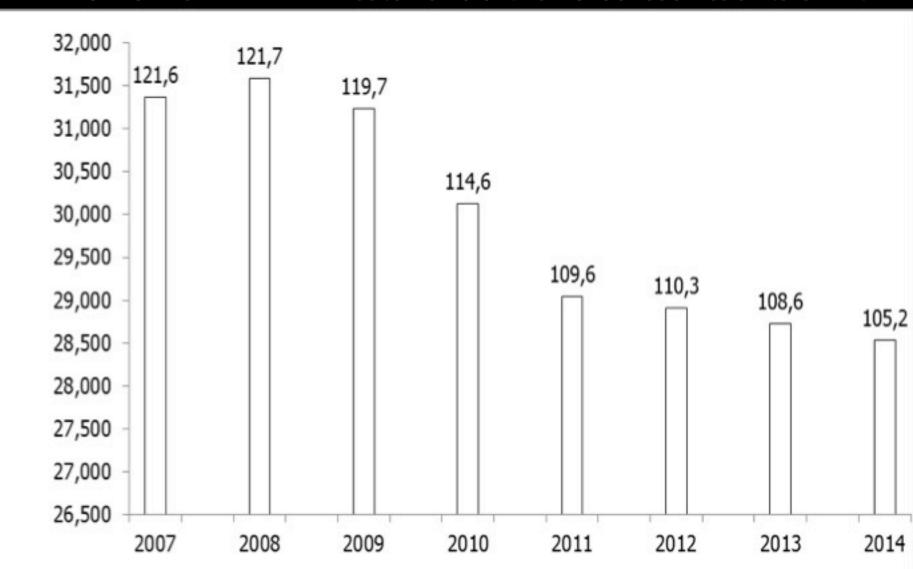
The Study on the incidence of hip fractures in Italy over 10-year period has started with Prof Tarantino and Iolascon during the ISBEM Summer School 2013 «Statistics and Pharmaco **Economics for Clinical Trials**» Your Juniors are welcome Every summer in Salento

A Really Positive Finding

- For the first time in Italy we have documented a reduction of hip fractures in women aged 65-74 years old between 2000 and 2014.
- The number of fractures and rates per 10,000 goes down to the lowest level documented since year 2000 (8718 fractures in 2014 vs. 9382 in year 2000).

Decreasing Trend Women 75-84

NEW UNPUBLISHED DATA - Piscitelli & Tarantino - Under Submission to OP Int

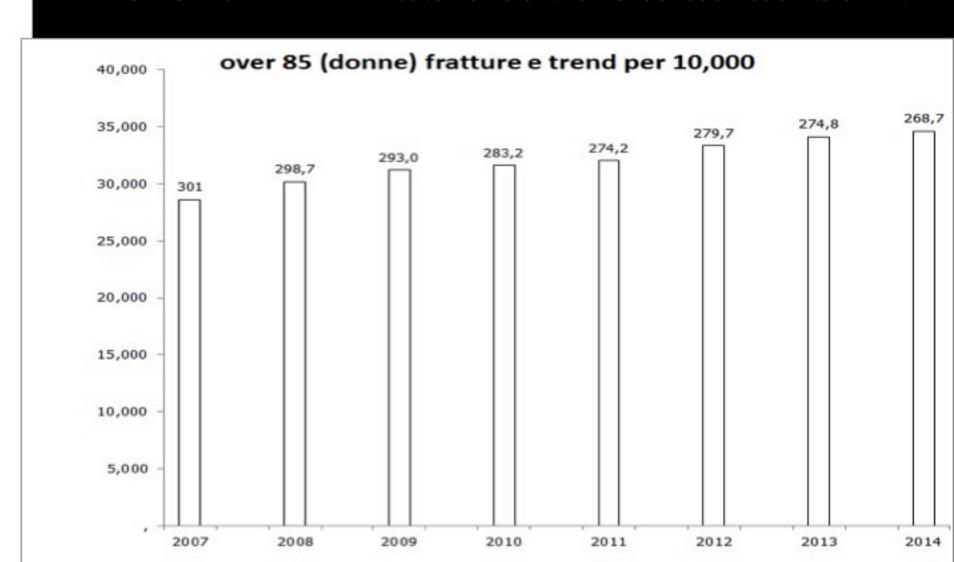


And Even More Positive

- The Reduction is observed in ALL the Regions up to 79 years old.
- The reduction is confirmed also in women aged 80-84 years old between 2007 and 2014 with the exception of Lombardia (+29% from 4312 to 5562), Calabria (+43% from 723 to 1036), Campania (+43.5% from 1535 to 2204) and Puglia (+28% 1503 to 1937)!

Decreasing Trend Women >85

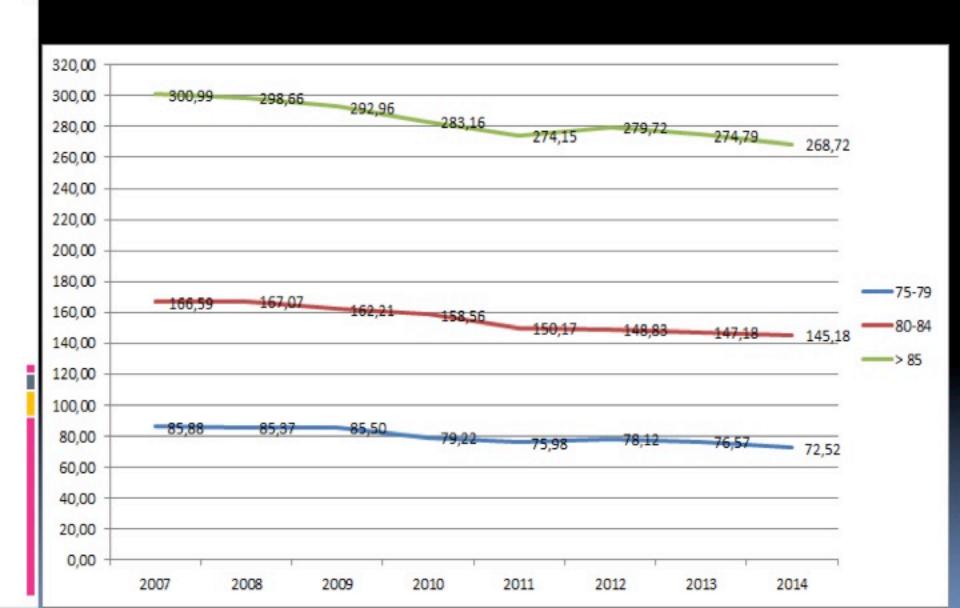
NEW UNPUBLISHED DATA - Piscitelli & Tarantino - Under Submission to OP Int



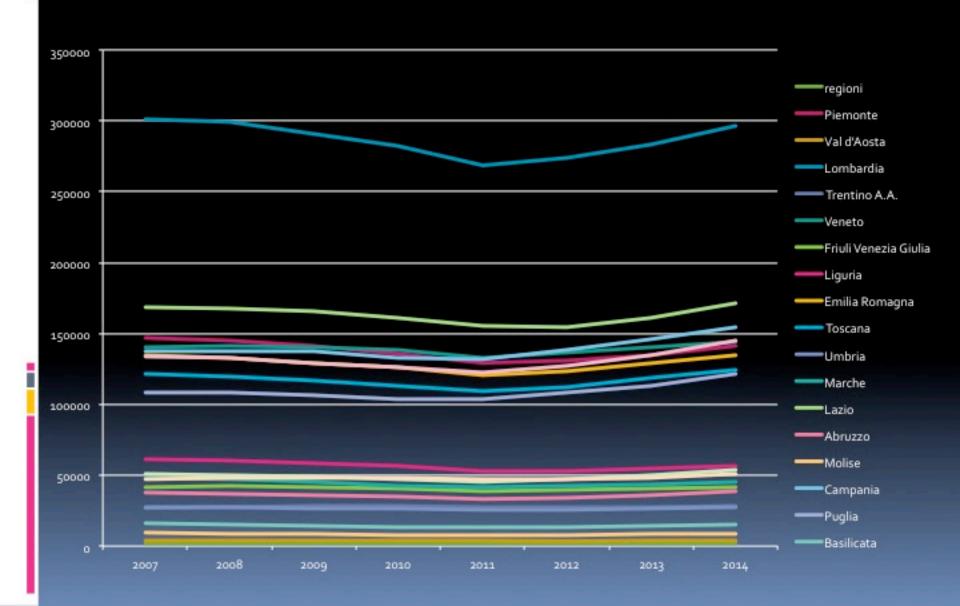
A paradox in people >85 ?

- Hip Fractures are dramatically increasing in all the regions from year 2007 to 2014 in people aged >85 years old with the exception of Lazio (-9.5% from 3382 to 3090).
- However the Rate per 10,000 is DECREASING at national level also in this latter age group.
- This is because the overall number of hip fractures is increasing BUT... it is not increasing at the same RATE of the population belonging to those age groups.

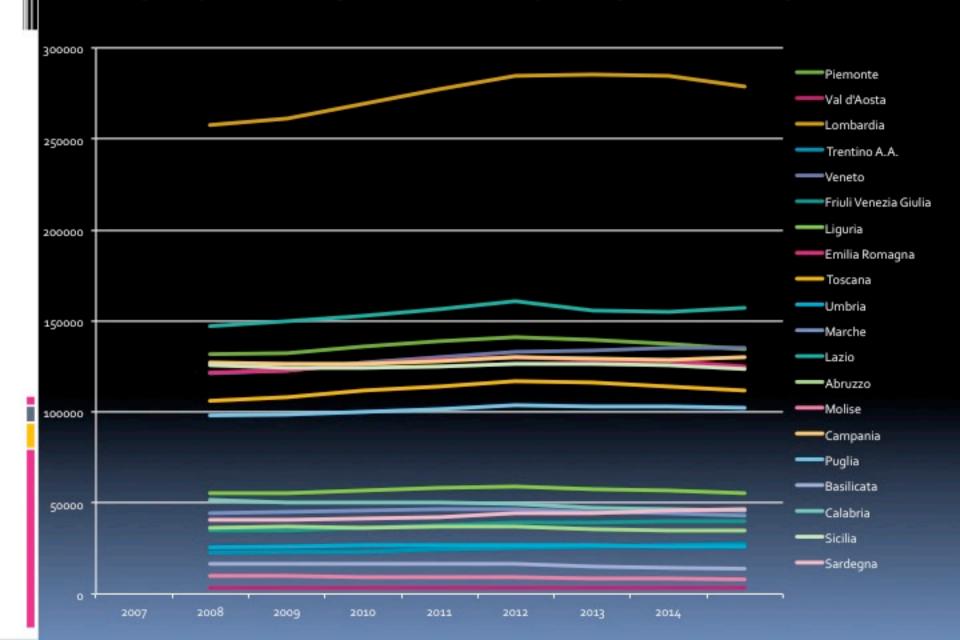
Summary per Age Group >75



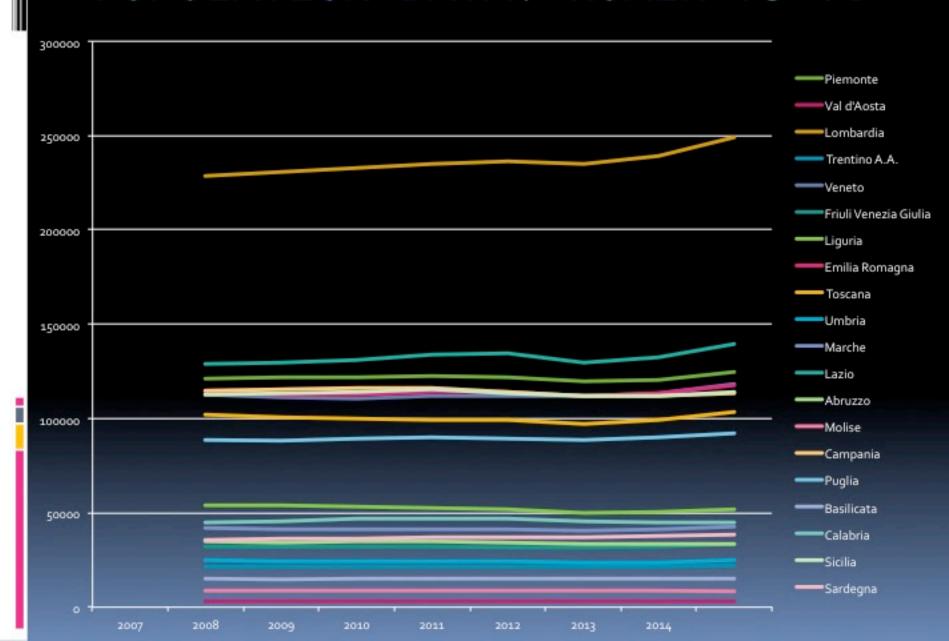
POPULATION DATA: WOMEN 65-69



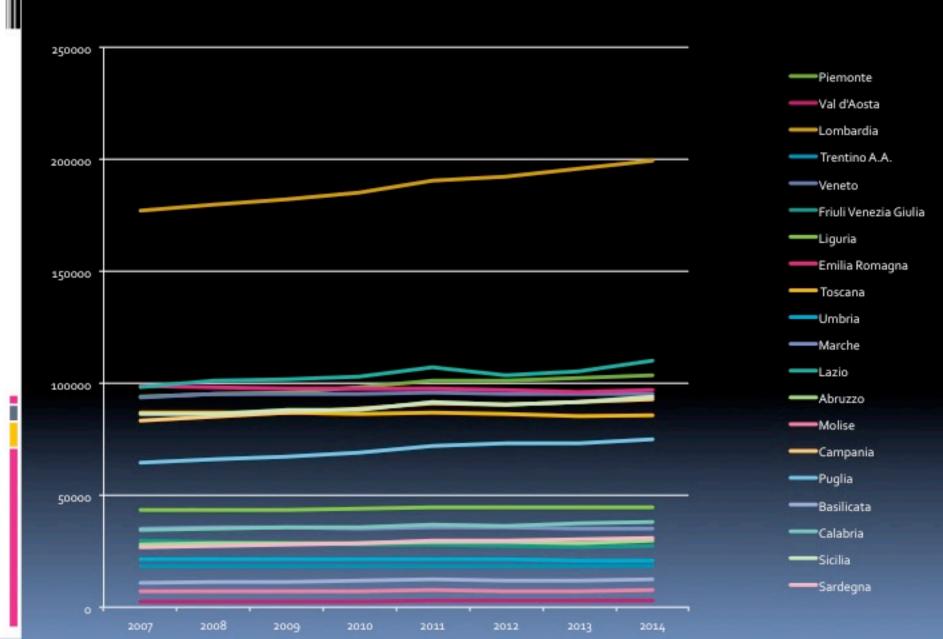
POPULATION DATA: WOMEN 70-74



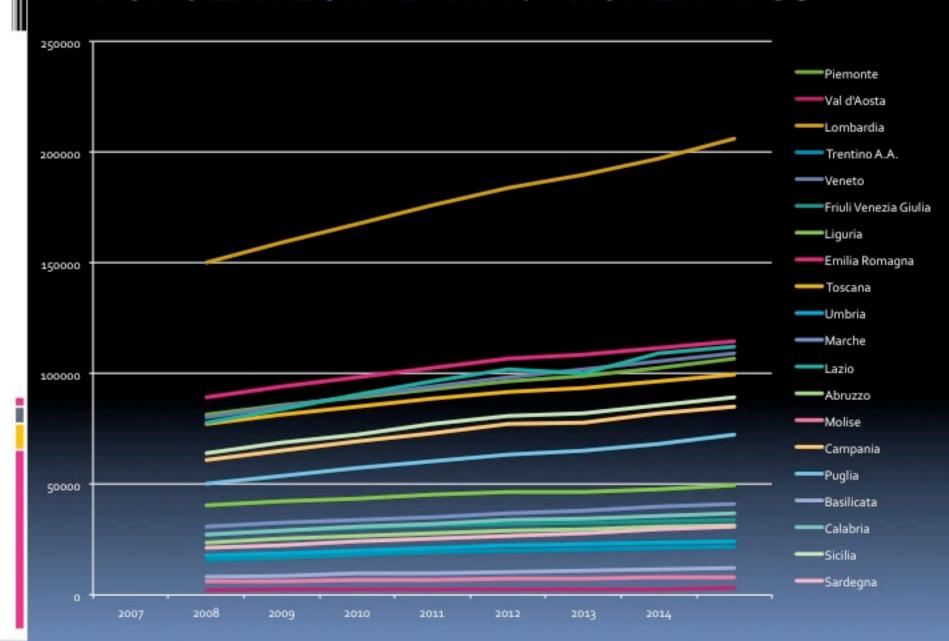
POPULATION DATA: WOMEN 75-79



POPULATION DATA: WOMEN 80-84



POPULATION DATA: WOMEN >85



SUMMARY

- We estimated a total of 741,633 hospitalizations due to hip fractures between 2007 and 2014 in people ≥65 (women: 568,203; men: 173,430), with an overall increase of 5.50% over the 8-year period (+3.36 in females and +12.9% in males).
- About 43.75% (n=324,459) of total hip fractures observed in people ≥65 years old were suffered by patients aged ≥85 years old. Women aged ≥85 accounted for 34.49% (n=255,763).

SUMMARY

- Between 2007 and 2014, the incidence rate per 10,000 inhabitants in people aged 65-74 decreased from 28.65 to 25.31 in women (– 13.02%) and from 13.41 to 11.65 in men (– 13.12%).
- Incidence per 10,000 in the age group 75-84 decreased from 121,6 to 105,2 in women (-13.49%) and from 55.8 to 47.5 in men (-14.87%).
- Also in people aged ≥85 the incidence per 10,000 declined over the entire study period from 300.99 to 268.72 in women (-10.72%) and from 174.59 to 171.17 in men (-1.96%).

EPIDEMIOLOGICAL PARADOX ?

- How can we explain the reduction in hip fractures rates up to 2014 in the frame of a general increase in the number of overall fractures which mostly concern people >85?
- A possible explanation for that should take into account all the efforts made since year 2000 in rising the awareness and treatment of OP.

GOOD JOB! BUT FOCUS ON HIGHER RISK!

General Considerations

Costs sustained for hip fractures occurring in people >65 years old (mostly women >80) are already higher than costs sustained for all the AMI occurred in adults aged >45 and are comparable to direct costs of strokes. Mortality is a common problem of all these three conditions.

ALWAYS TREAT PEOPLE >80

The Paradox of «MINOR» OSTEOPOROTIC FRACTURES

- Only 20-30% of these very common fractures leads to symptoms or medical attention (the so called «clinical vertebral fractures»)
- The EPOS study estimated that over 65 y.o. 1 woman out 3 has a vertbebral fracture.

The Italian ILSA study estimated that 25% of Italian women >65 anni has a vertebral fracture: estimated prevalence: 1.500.000 cases.

- Our Study estimated 150.000 new overall vertebral fractures in Italian people >65 years old (including non symptomatic fractures)
- About 50.000 of those are clinical vertebral fractures leading to medical attention at emergency departments and 15.000 need hospital admission.

Estimated costs of the overall 150.000 new annual cases of vertebral fractures (including hospitalizations and surgery) is estimated at 300 million euros per year.

THE OTHER «MINOR» FRACTURES

- Fractures of the Humer are the second most common fracture event after 65 years old. They increase by 5 folds the risk of hip fractures.
- Our Italian study estimated **48.000** the new annual cases of humer fractures. About **10.000** of these fractures lead to hospitalization. Total costs estimated for these fractures are 85 Million Euros per year.

TARANTINO, Piscitelli et al. Arthritis Res. & Therapy 2010

THE OTHER «MINOR» FRACTURES

- Each year in Italy 85.000 people experience a wrist/ distal radius fracture. About 13.000 of these fractures result in hospital admission determining costs for 88 million Euros.
- New ankle fractures per year are 35.000 (14.000 leading to hospitalization) with estimated costs of 80 million Euros.
- 44.000 rib fractures, 13.000 clavicle, 10.000 scapula, 9.000 pelvis e 7.000 tibial fractures

TARANTINO, Piscitelli P. et al. Arthritis Res. & Therapy 2010

DIRECT COSTS OF NON HIP FRACTURES «MINOR OSTEOPOROTIC FRACTURES»

Year	People >65 With Vertberal Fractures	People >65 With Humer Fractures	People >65 With Wrist Fractures	People >65 With Other Fractures	Total COSTS
	MILLION EUROS	MILLION EUROS	MILLION EUROS	MILLION EUROS	Million Euros
2006	300	85	88	150	623

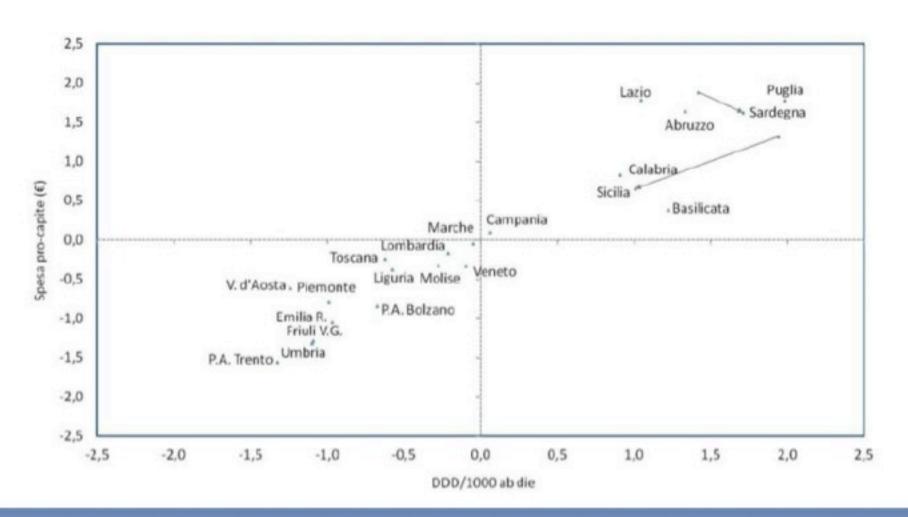
THE PARADOX OF PHARMACEUTICAL COSTS

COSTS FOR ANTIFRACTURE DRUGS (AIFA Note 79 - OSMED 2015)

- Antifractures drugs in Italy can be prescribed with costs sustained by NHS only under AIFA Note 79. They represent the 6% (216 million Euros in 2015 but 363 million Euros in 2010) of the total costs attributable to drugs prescribed under AIFA notes (3.6 Billion out of 13.4 Billion of National Pharmaceutical Expense – 23%);
- Antifracture drugs prescribed under AIFA 79 Note account for 1,6% of the National Pharmaceutical Expense (2.6% nel 2010). Cardiovascular drugs account for 22% (3.4 Billion).

AIFA 79 Costs per Region

Figura 7.2.10c. Farmaci per l'osteoporosi, variabilità regionale dei consumi farmaceutici 2015 per quantità e spesa pro capite e variazione rispetto all'anno precedente (valori standardizzati rispetto alla media nazionale)



THE PARADOX OF PREVENTION

We know that 623 million Euros are spent to treat non hip fractures.

It will cost **80 milion Euros** to treat (with an antifracture therapy leading to a reduction of fracture risk) all the **300.000** people that each year experience a vertebral, humer, wrist, ankle, tibial and other fragility fractures.

Is it so much or too low?

THE PARADOX OF PREVENTION

This amount of money corresponds to the 0,57% of the National Pharmaceutical Expense but would result in 85 million Euros Savings taking into account the costs of the drugs, avoiding about 100.000 fractures per year.

THE PARADOX OF PREVENTION

- Even more cost-effective is the case of people >65
 years old who experience a hip fractures generating 1
 billion Euros of direct costs per year. We would need
 18 milioni Euros to treat each year all the new hip
 fractured patients. (these people have the right to
 receive treatment under AIFA code 79!). Again: is it
 too much?
- It is only the **0.13% of the National Pharmaceutical Expense** but would result in reduction of hip refractures (up to 30%) and other new fractures (5-10%) and direct costs savings estimated at **43** million Euros per year, taking into account the cost of the drugs in case of 100% compliance.

The Paradox of Prevention: What we do now

- Only the 13% of hip fractured patients is currently treated with antifracture drugs: 9.200 patients assuming a reimbursed therapy (2,5 million Euros of costs for the NHS in case of 100% compliance).
- We are now spending the 0,017% of the national pharmaceutical expense!
- Moreover, only 30% of patients with hip fracture present an optimal compliance (>80% at 1 year), which represent another PARADOX: the paradox of DRUG EFFICACY LOSS due to uncompliant treatments that means waste of money!

The Parox of Compliance: Use Case TUSCANY

- 16 million Euros spent for antifracture therapies: too much? And the Compliance which drives efficacy?
- <u>53 Million spent for Statins</u>, 9% of the Regional Pharamaceutical Expense, with a 9-month compliance only of 38%, while 15% of patients receive only 1 box per year. Waste= 53%

Compliance Antifracture Drugs

	Compliance	Age group	% Patients per age group over total pazients	Alendronate	Risedronate	Strontium ranelate	Alendronate + colecalciferol	Ibandronate	Neridronate	
			95.270	(26,71% on total patients)	(21,11% on total patients)	(18,19% on total patients)	(17,96% on total patients)	(8,79% on total patients)	(4,56% on total patients)	
1		0.0	70		5 500		20	5n 7g	102 102	
		60/70	21,47%	91,60%	92,96%	86,46%	92,21%	92,87%	22,31%	
	1 Months	70/80	37,02%	92,83%	93,64%	86,71%	92,86%	93,05%	25,18%	
Į		80/90	28,95%	92,94%	93,07%	84,33%	91,05%	92,43%	25,53%	
1					y	100 240		91	355 — 356 — 1 355 — 6	
_		60/70	21,47%	69,93%	75,49%	55,66%	70,28%	73,64%	0,00%	
	6 Months	70/80	37,02%	73,79%	76,37%	54,59%	72,32%	73,81%	0,00%	
		80/90	28,95%	73,85%	75,26%	49,33%	70,49%	72,14%	0,46%	
I.		- 34 - 14 (1)			2 77					
		60/70	21,47%	64,58%	70,36%	49,06%	63,96%	69,04%	0,00%	
	9 Months	70/80	37,02%	68,90%	71,87%	47,50%	67,31%	69,01%	0,00%	
I		80/90	28,95%	69,27%	71,19%	42,77%	65,19%	67,39%	0,28%	
1		(T)						F		
		60/70	21,47%	58,38%	65,73%	42,49%	58,33%	64,86%	0,00%	
	1 Year	70/80	37,02%	63,18%	66,90%	40,67%	61,52%	64,83%	0,00%	
		80/90	28,95%	63,70%	66,26%	35,86%	59,43%	62,39%	0,00%	

Compliance hip fractured pts: 30%

Compliance	Age groups			Risedronale		Strontium ranelate		Alendronate + collecaliciferol		Ibandronate		Naridronata		Teriponaticle		Zolendranete		Raloxifun		Clodrorete		Parathyroid Hormona	
											on total patients					Number of patients						Number of patients	
		237	17,70%	312	23,30%	419	33,53%	195	14,56%	82	6,12%	30	2,24%	28	2,09%	3	0,22%		0,00%	3	0,22%		0,00%
1 Months	60/70		100,00%		100,00%		100,00%		100,00%		100,00%		0,00%	۰			100,00%	c	0,00%		0,00%	c	0.00%
	70/80 80/90		100,00%		100,00%		100,00%		100,00%		100,00%	10	0,00%	12		9	0,00%	o o	0,00%	,	0,00%	0	0.00%
3 Months	60/70	15	80,00%	21	61.50%	30	78,26%	15	40.00%	11	63,64%	2	0,00%			1	100,00%		0,00%	1	0,00%		0,00%
3 11011113	70/80 80/90	73 130	68,49% 57,69%	101 160	78.22% 63,76%	134 231	73,79%	57 102	77.19% 56.86%	31 33	74,19%	10 15	0.00%	14 12			0,00%		0.00%	1	0.00%		0.00%
			46,67		47,62		81,25 %	15	26,67	11	64,00	ļ					400.000						1
6 Months	70/80	73		101		134	62,12%	57	50.88%	31	58,00%	10	0.00%	14	61.54N	2				1			0.00%
	80/90	130		160	45.675	231	63,06%	102	46.08%	33	-	15	0,00%	12	41,67%		0,00%		0,00%	1	0,00%		0.00%
9 Months	60/70	15	33.35%	21	47.62%	30	50,00%	15	20.00%		54.55%	2	0,00%	-		1	100,00%		0,00%	1	0,00%		0.00%
	70/80 80/90	73 130	38,36%	160	35,29%	134 231	45,97% 45,24%	57 102	58.00% M. 20%	31 31	48,20%	10	0,00%	14 12			0,00%		0,00%	1	0,00%		0.00%
HTELESCO DE			13.33		38,10		31.25		20,00														
1 Vear	60/70 70/80	15 79		21		30 134	%i 21.249	15 57	% 29.07%	11 31	16,16%	10	0.00%	14	0,00% 75,00%	1 2				1			0.00%

CONCLUSIONS: Take Home Messages

- Focus on Higher Risk Patients: Treat always >80 y.o.
 - and treat always previously fractured patients
- Use Algorithms (Frax/Defra) in non higher risk pts.
- Consider compliance issue ALWAYS (or waste money)
- Knowledge Transfer Exchange from Researchers to Decision Makers (Drive Regional Policies on OP)
- Pilot Project s at Regional Level

THANKS

- Prof. F. Vescini
- Prof. U. Tarantino
- Prof. G. Iolascon
- Prof. A. Distante
- Speakers and Chairmen of the Conference

THANKS TO EVERYBODY FOR THE ATTENTION