



BONE FRACTURE

KDIGO

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Division of Comprehensive Geriatrics in Community,
Niigata University Graduate School of Medical and Dental Sciences

OUTLINE

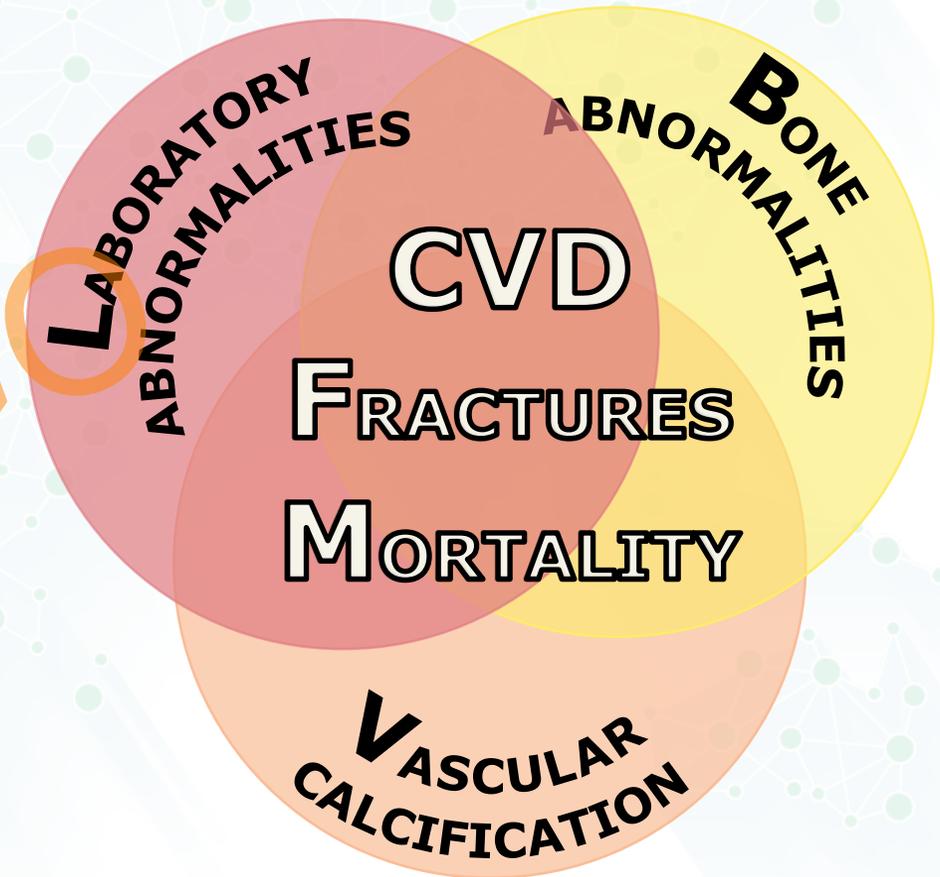
Hip fracture

- Poor survival
- GP and Dialysis pts
- Regional variation
- Dialysis modality
- Trend

Vertebral fracture

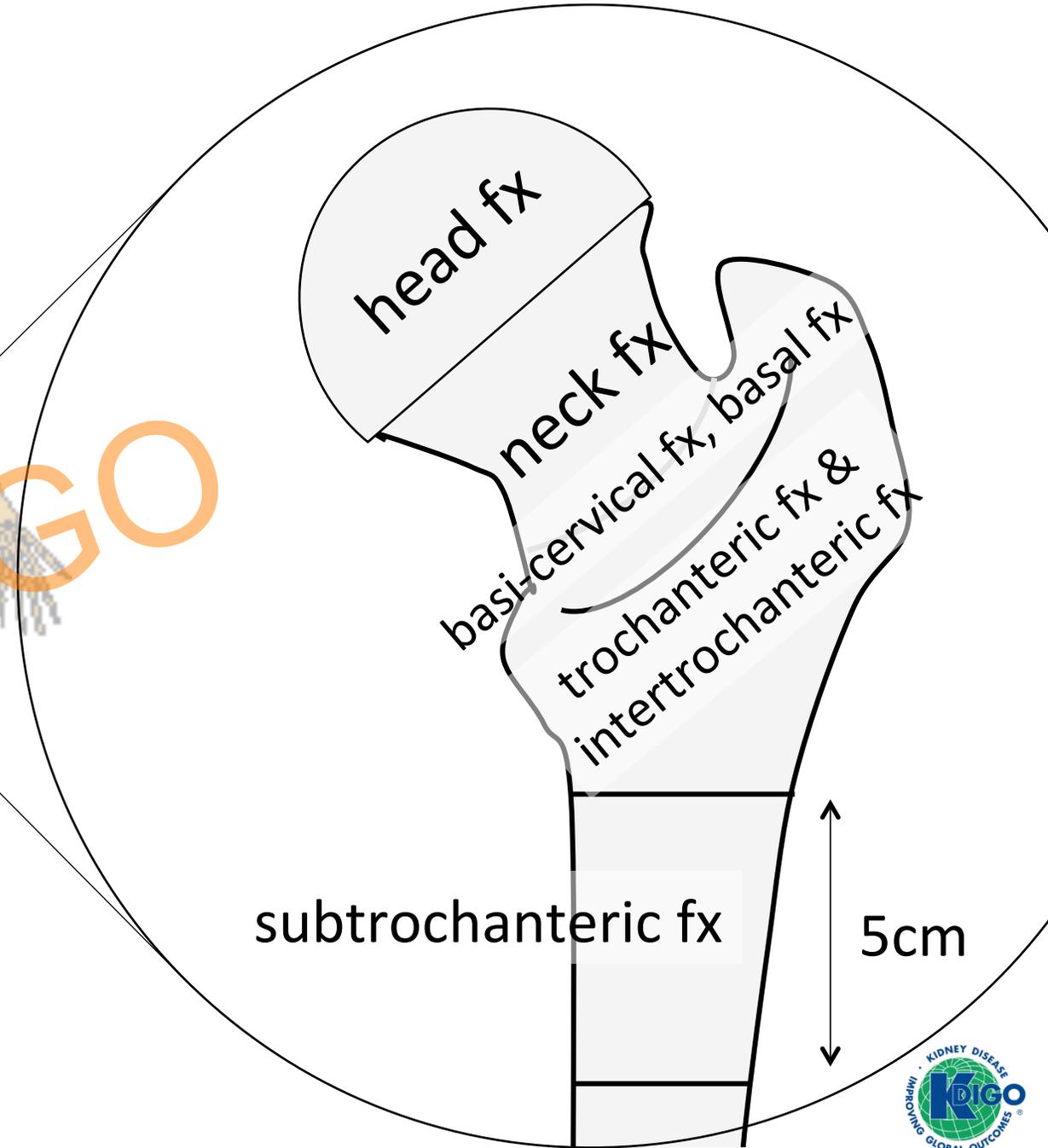
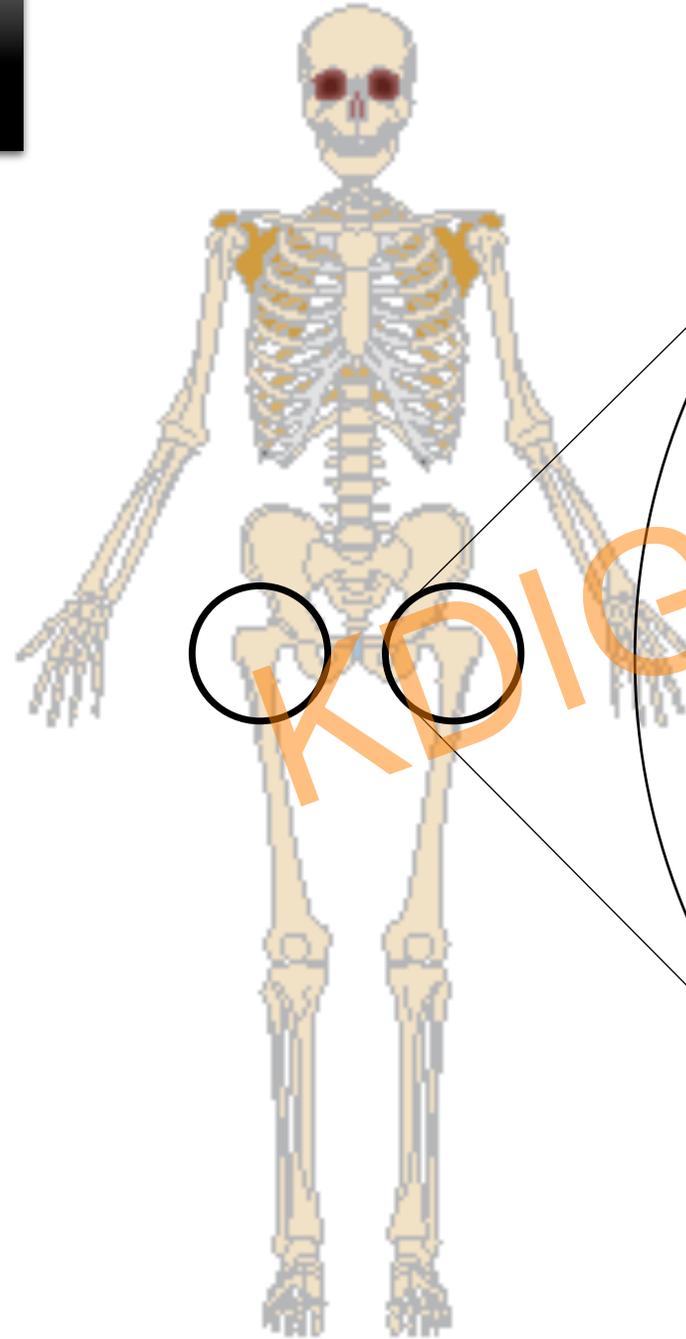


CHRONIC KIDNEY DISEASE MINERAL AND BONE DISORDER



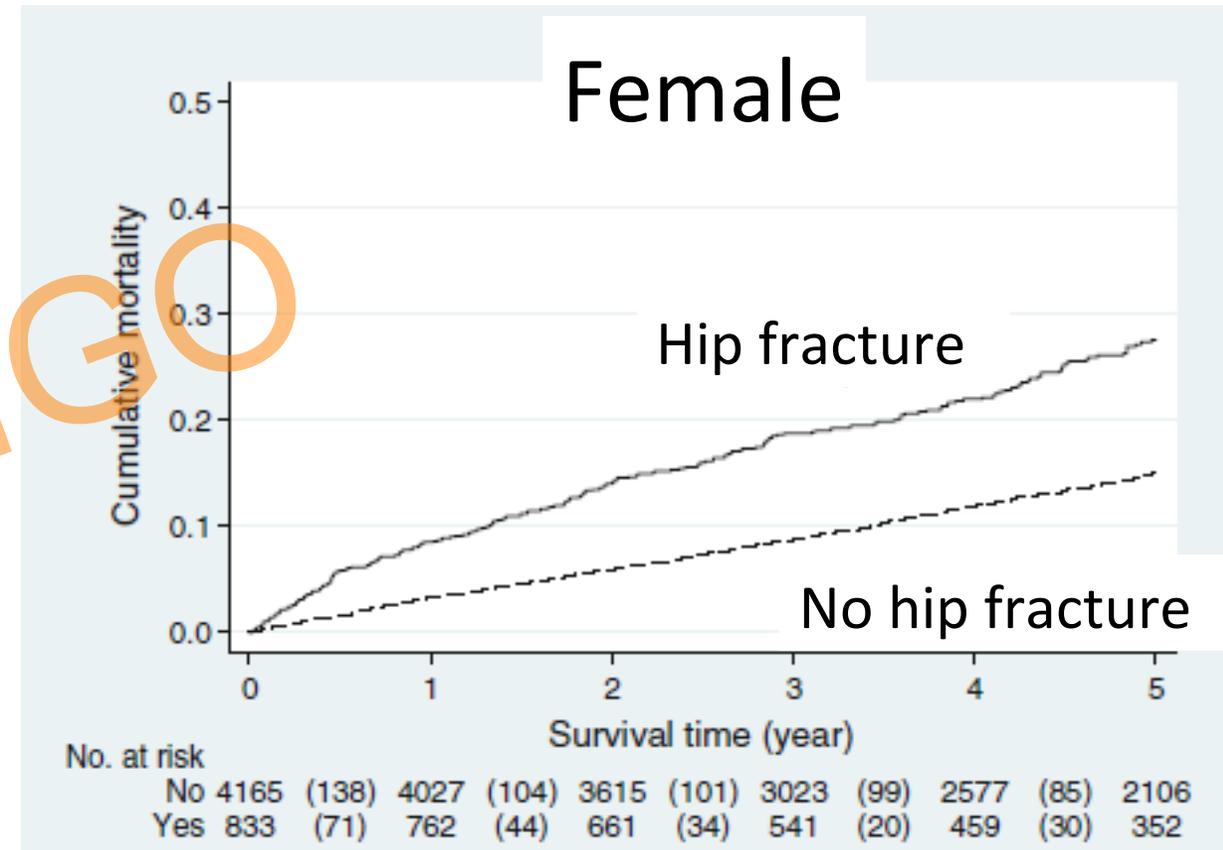
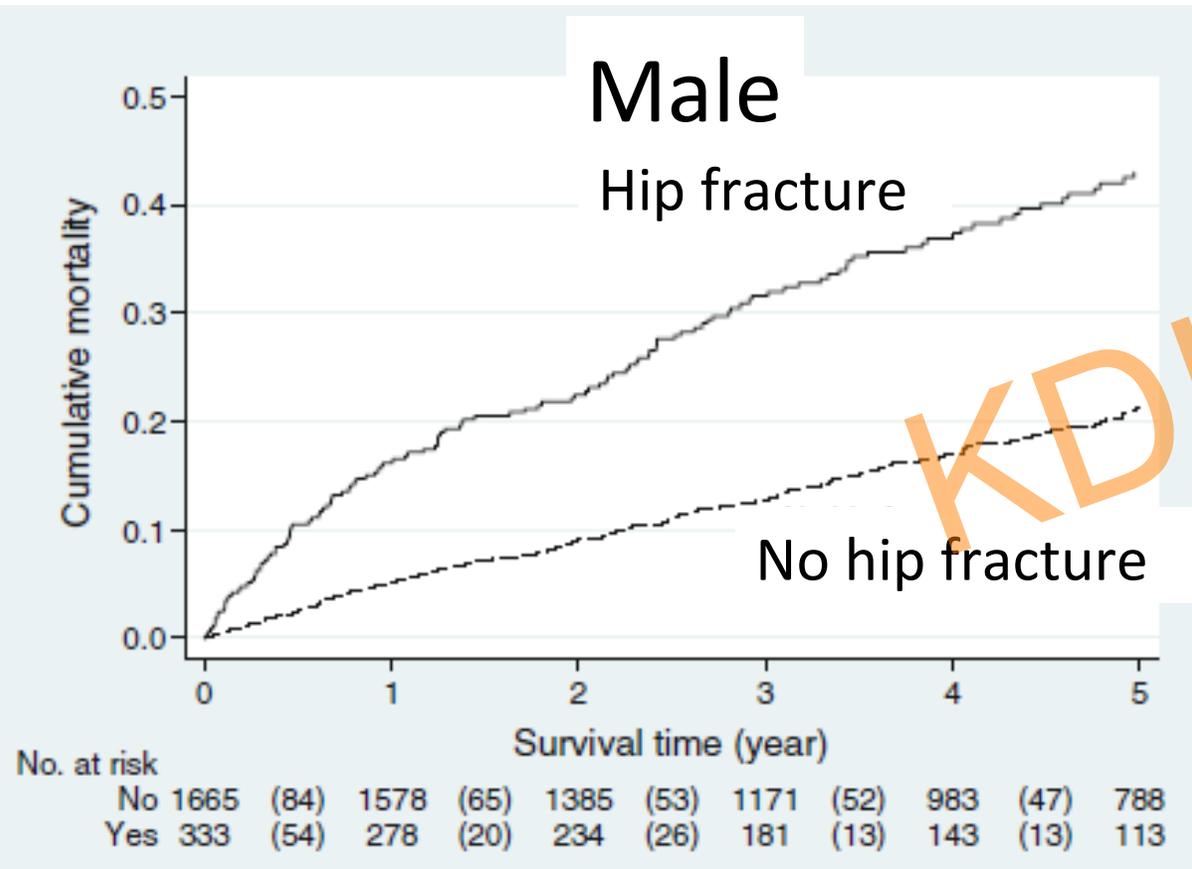
CKD-MBD

Hip fracture



HIP FRACTURE IS ASSOCIATED WITH POOR OUTCOME IN THE GENERAL POPULATION

Koh GC, et al. *Osteoporos Int.* 2013;24:1981-9.

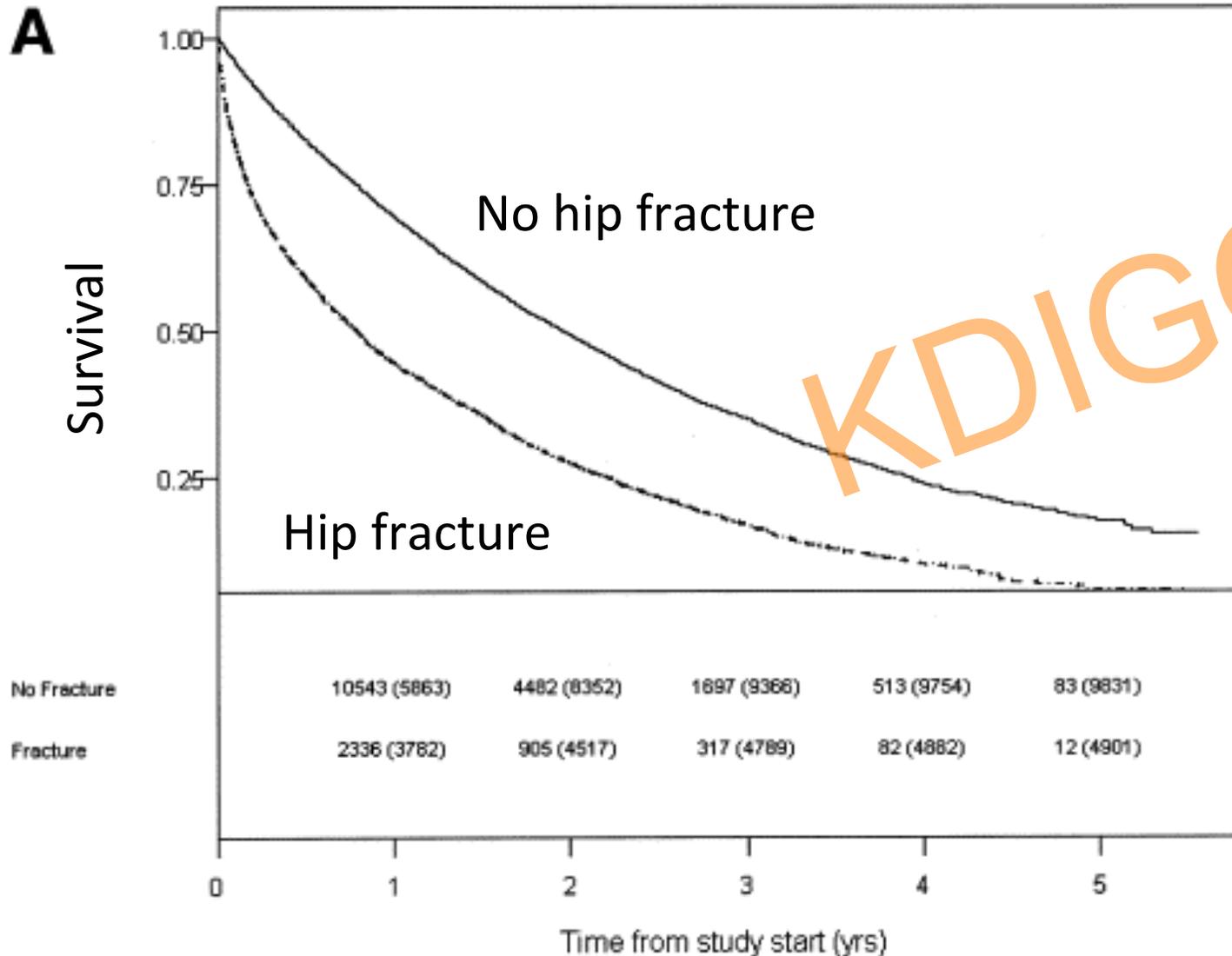


The Singapore Chinese Health Study, a population-based cohort of 63,257 middle-aged and elderly Chinese men and women in Singapore recruited between 1993 and 1998.

HIP FRACTURE IS ASSOCIATED WITH POOR OUTCOME AMONG DIALYSIS PATIENTS

Mittalhenkle A, et al. *Am J Kidney Dis.* 2004;44:672-9.

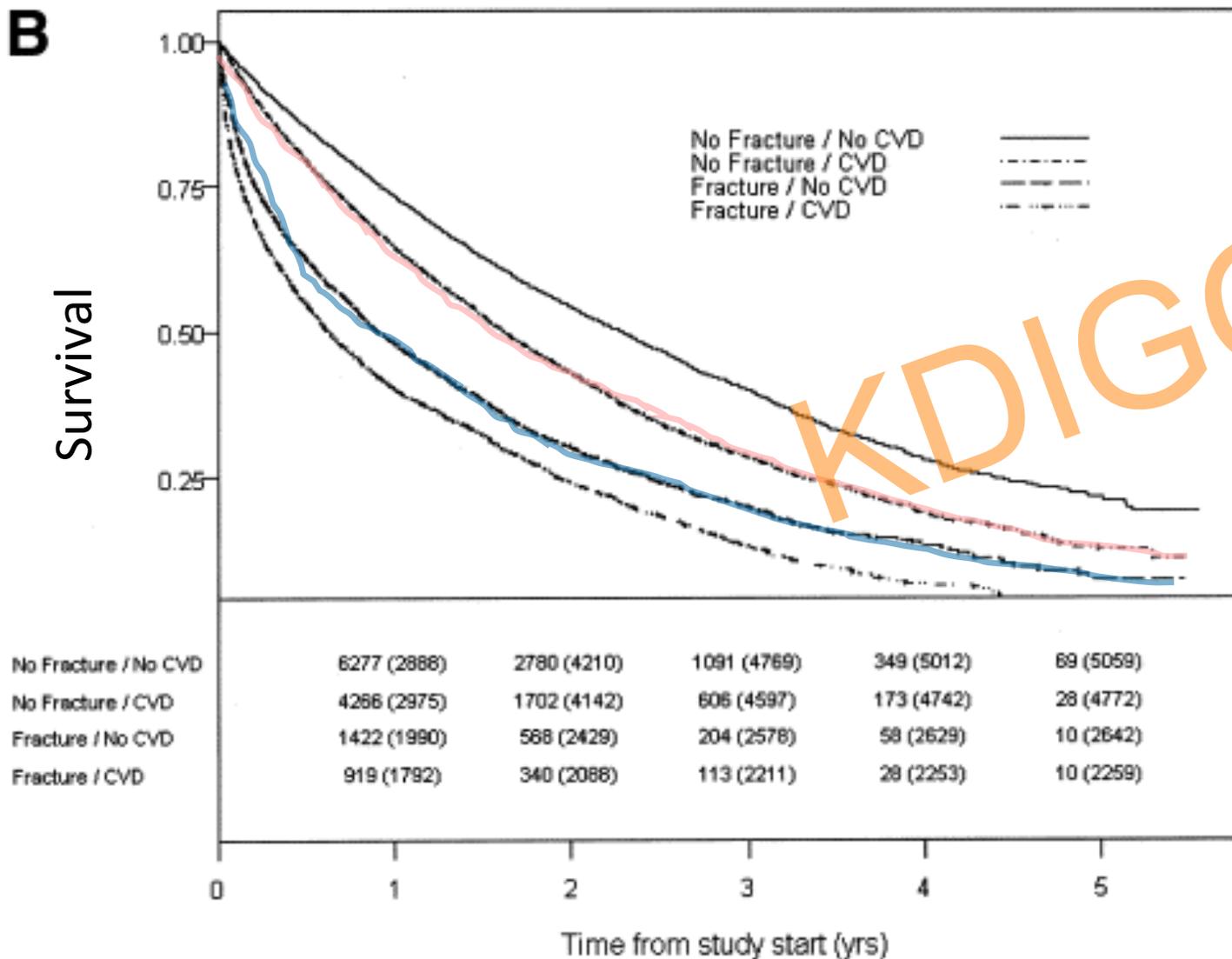
A matched cohort study of dialysis patients using data from the USRDS



HIP FRACTURE IS ASSOCIATED WITH POOR OUTCOME

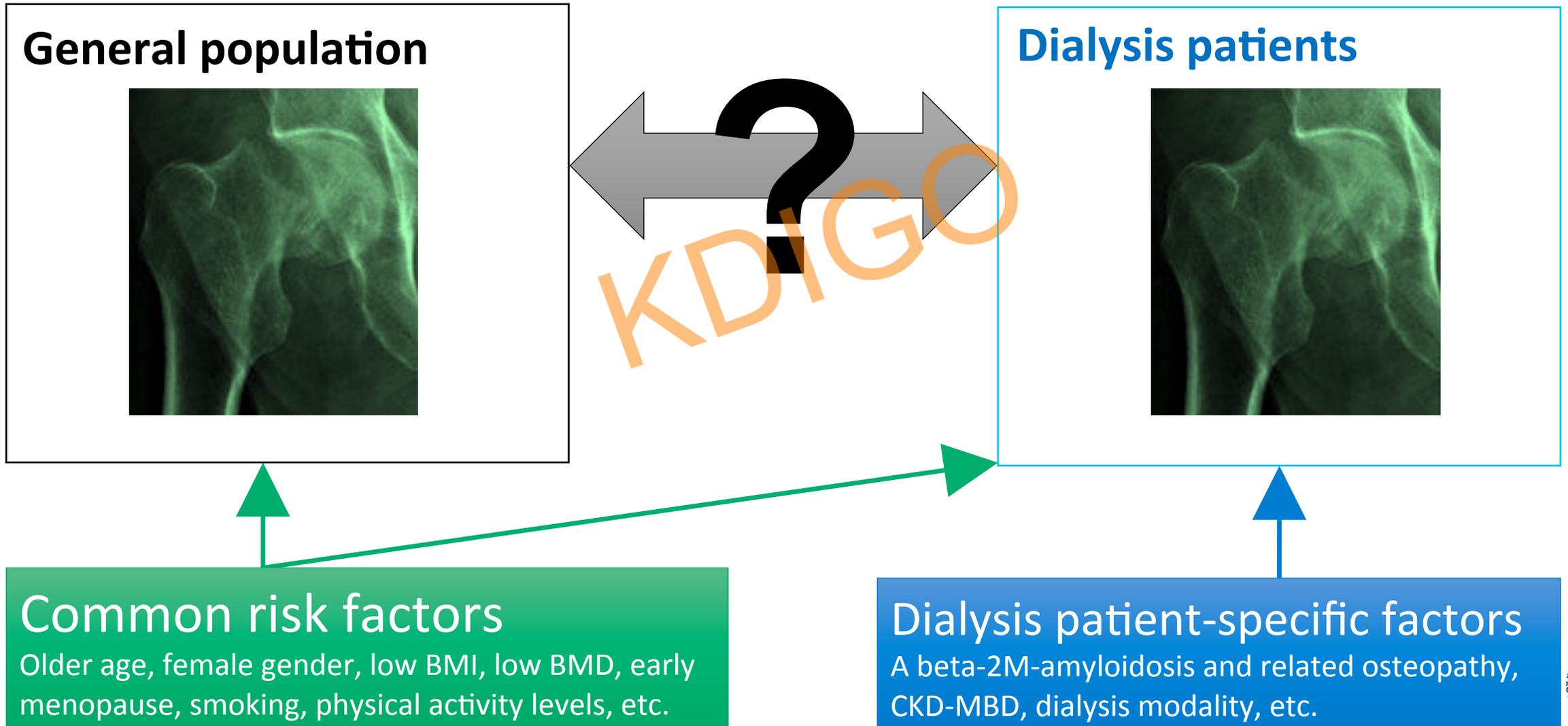
Mittalhenkle A, et al. *Am J Kidney Dis.* 2004;44:672-9.

A matched cohort study of dialysis patients using data from the USRDS



No fracture/No CVD
 No fracture/CVD
 Fracture/No CVD
 Fracture/CVD

DIALYSIS PATIENTS HAVE MORE RISKS OF HIP FRACTURE COMPARED WITH THE GENERAL POPULATION



4 TIMES HIGHER THAN THAT OF THE GENERAL POPULATION.

General population



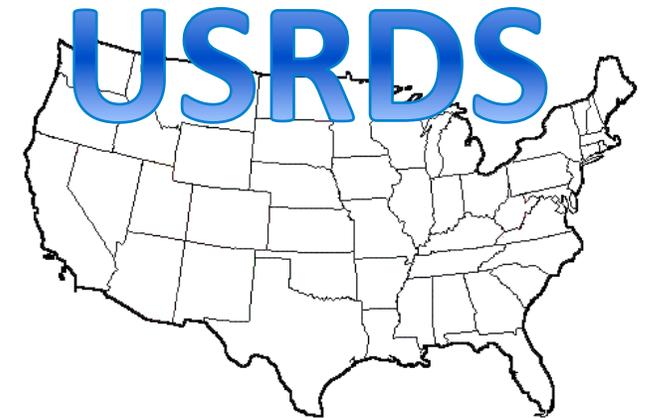
Hip fracture incidence among American Caucasian populations from 1983 to 1992.



This study included only Caucasians.

How about Asians?

Dialysis patients



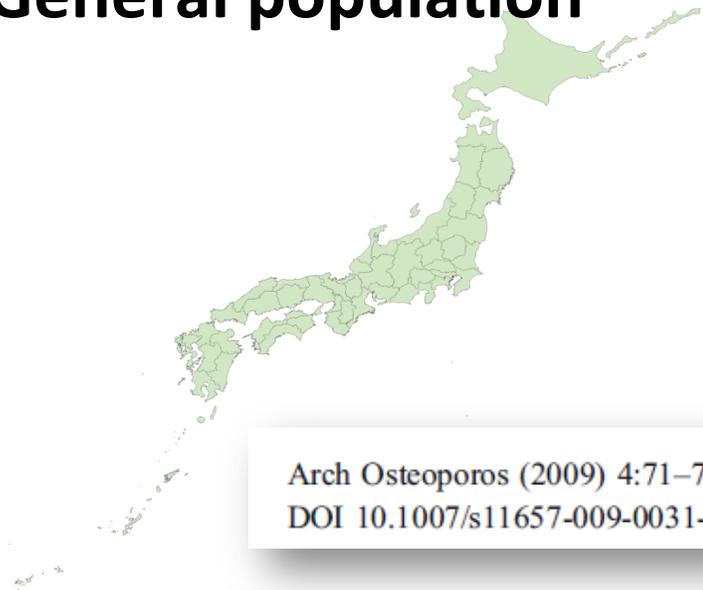
Hip fracture incidence among all Caucasian patients who began dialysis between 1989 and 1996

DIALYSIS PATIENTS HAVE DEFINITELY HIGHER RISK OF HIP FRACTURE COMPARED WITH THE GENERAL POPULATION

Wakasugi M, et al. *J Bone Miner Metab.* 2013;31:315-21.

INCIDENCE: 11.3/1,000 PATIENT-YEARS
(95% CI, 10.7 TO 11.9)

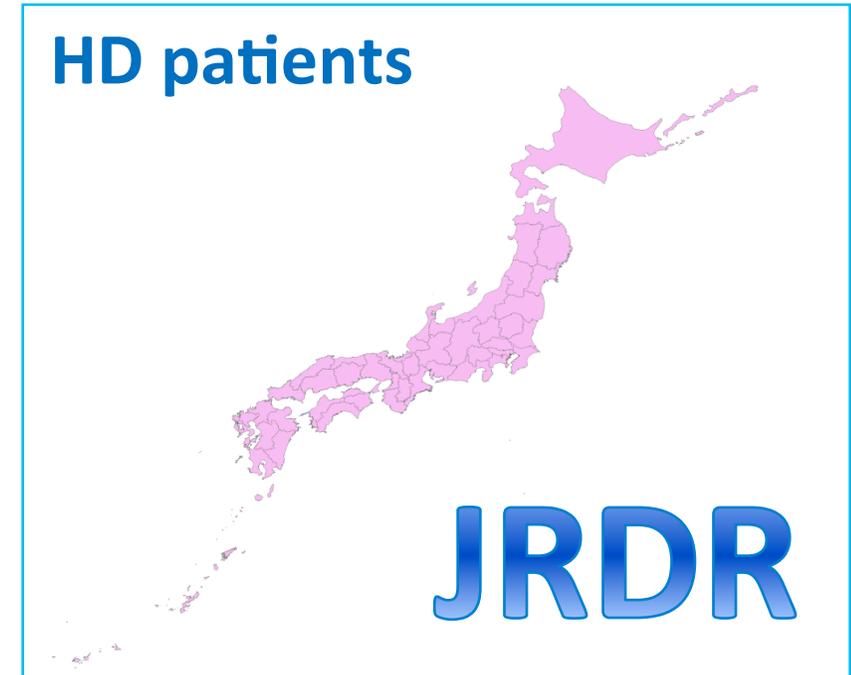
General population



Hip fracture incidence among Japanese general population



HD patients

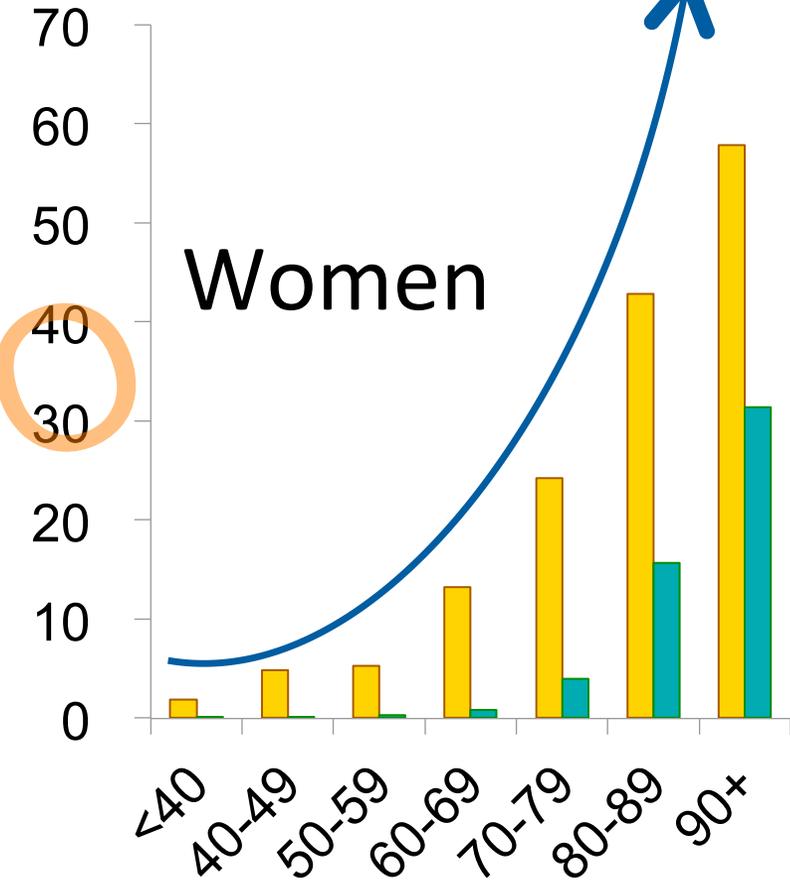
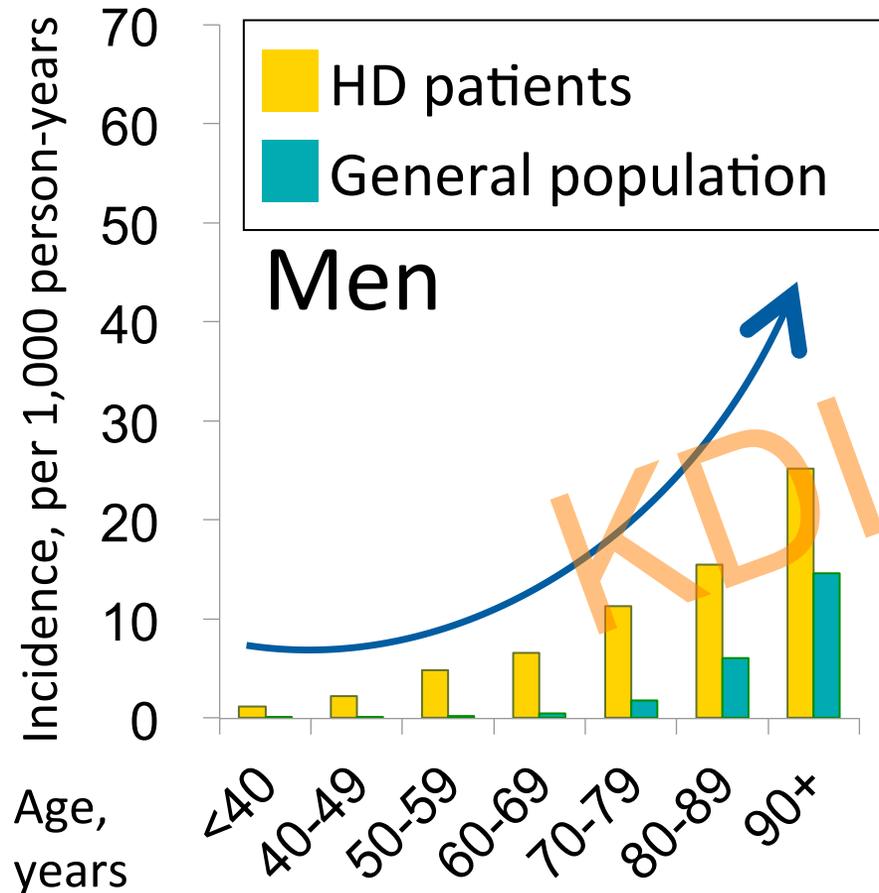


Hip fracture incidence among Japanese HD patients

JRDR: the Japanese Society for Dialysis Therapy Registry



THE OVERALL INCIDENCE OF HIP FRACTURE AMONG JAPANESE HD PTS WAS 5- TO 6-FOLD GREATER THAN IN THE GENERAL POPULATION.

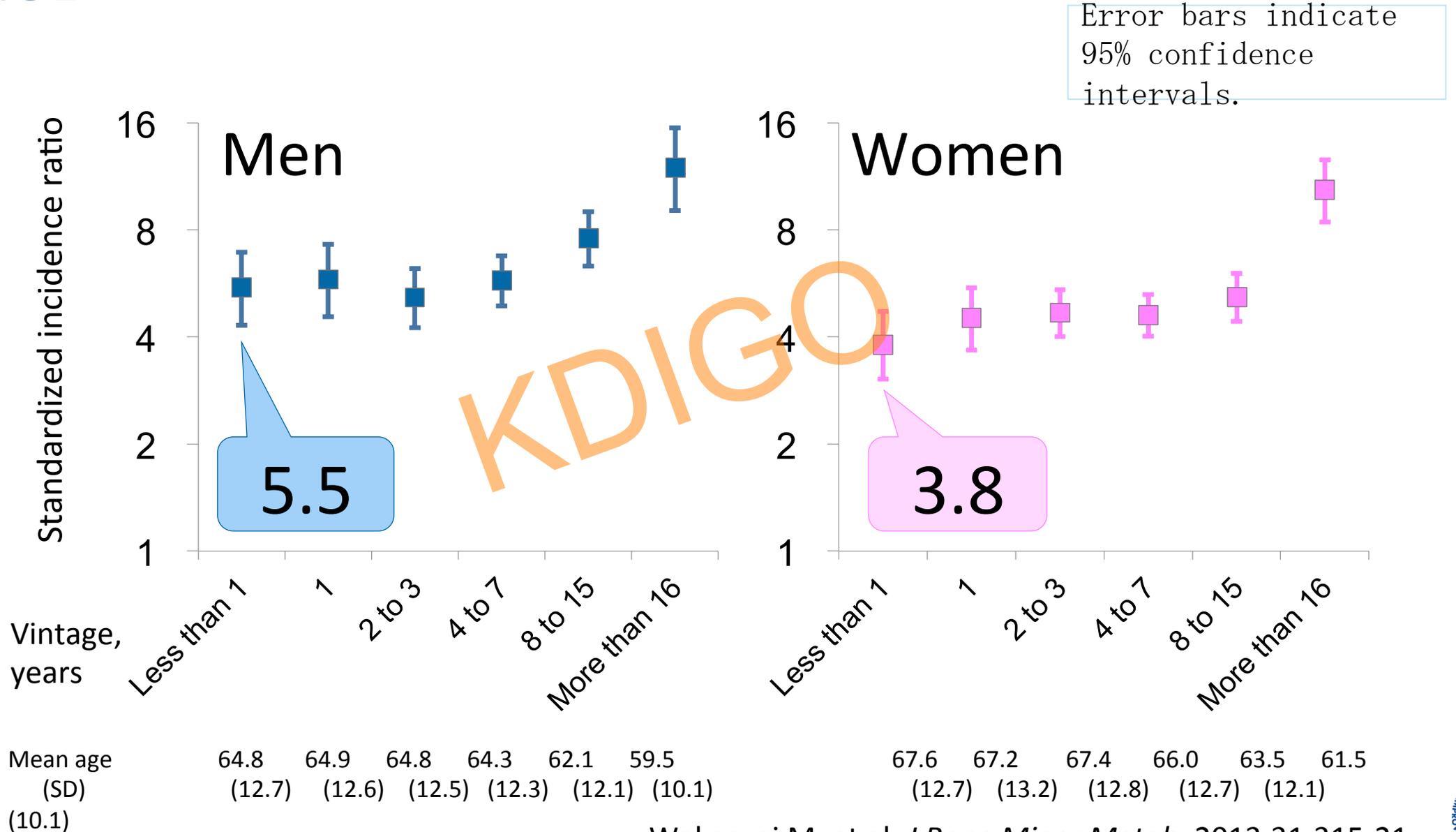


Standardized Incidence Ratio

6.2 (95%CI 5.7 - 6.8)

4.9 (95%CI 4.6 - 5.3)

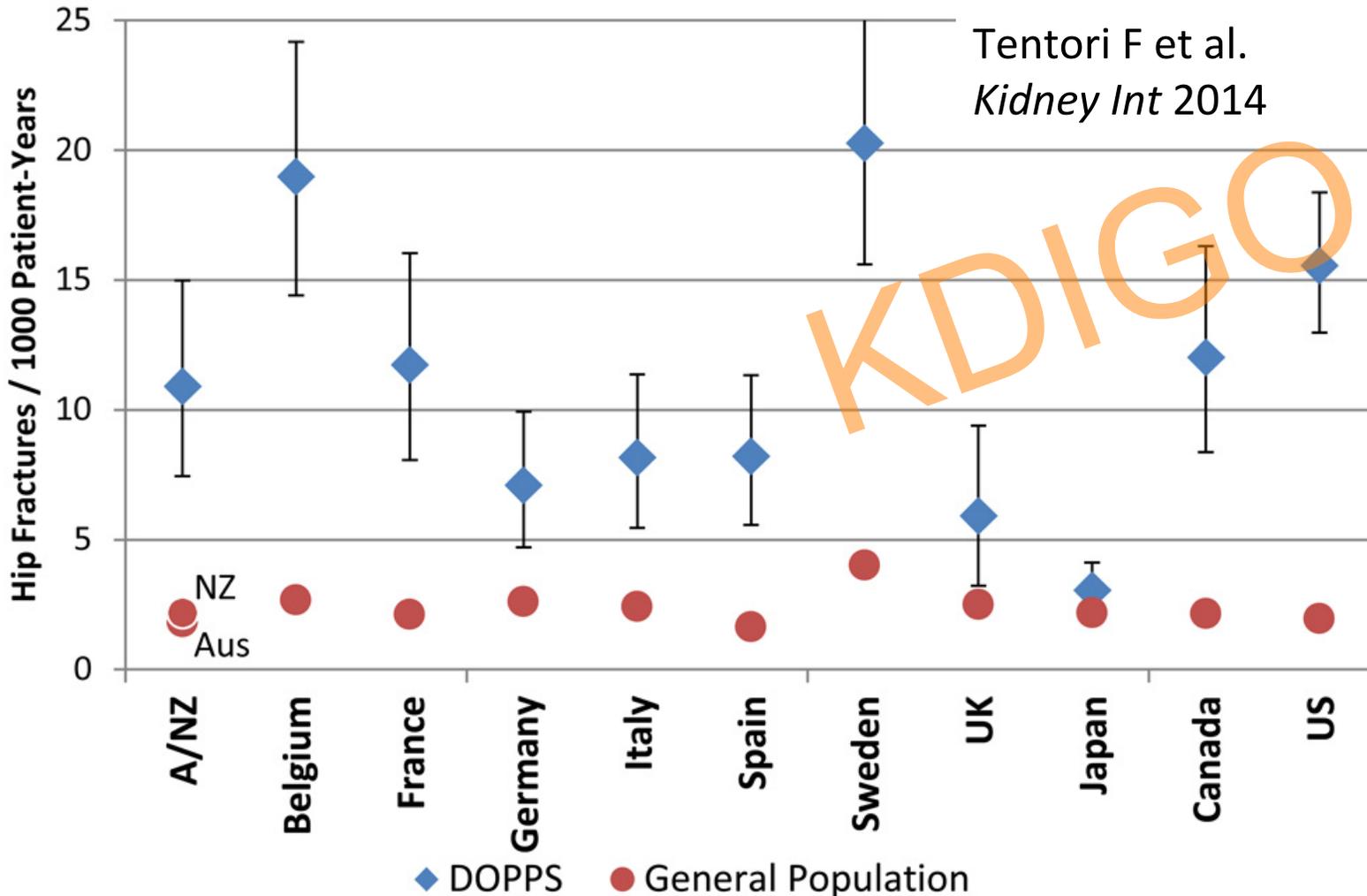
VINTAGE



Wakasugi M, et al. *J Bone Miner Metab.* 2013;31:315-21.



THE COUNTRY-SPECIFIC RATE FOR HIP FRACTURE IN THE DIALYSIS POPULATION IS HIGHER THAN REPORTED RATES FOR HIP FRACTURE IN THE GENERAL POPULATION.



Dialysis patients face higher risks for hip fracture compared to the general population.

TAIWAN NATIONAL COHORT STUDY

1903 PATIENTS HAD A HIP FRACTURE (INCIDENCE: 89.21/10,000)

Bone 64 (2014) 235–239

Lin ZZ, et al. *Bone* 2014;64:235–239



Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone



Original Full Length Article

Epidemiology and mortality of hip fracture among patients on dialysis:
Taiwan National Cohort Study



Zhe-Zhong Lin ^{a,1}, Jhi-Joung Wang ^{b,1}, Chi-Rung Chung ^c, Po-Chang Huang ^c, Bo-an Su ^{d,e}, Kuo-Chen Cheng ^{a,f},
Chung-Ching Chio ^g, Chih-Chiang Chien ^{h,i,*}

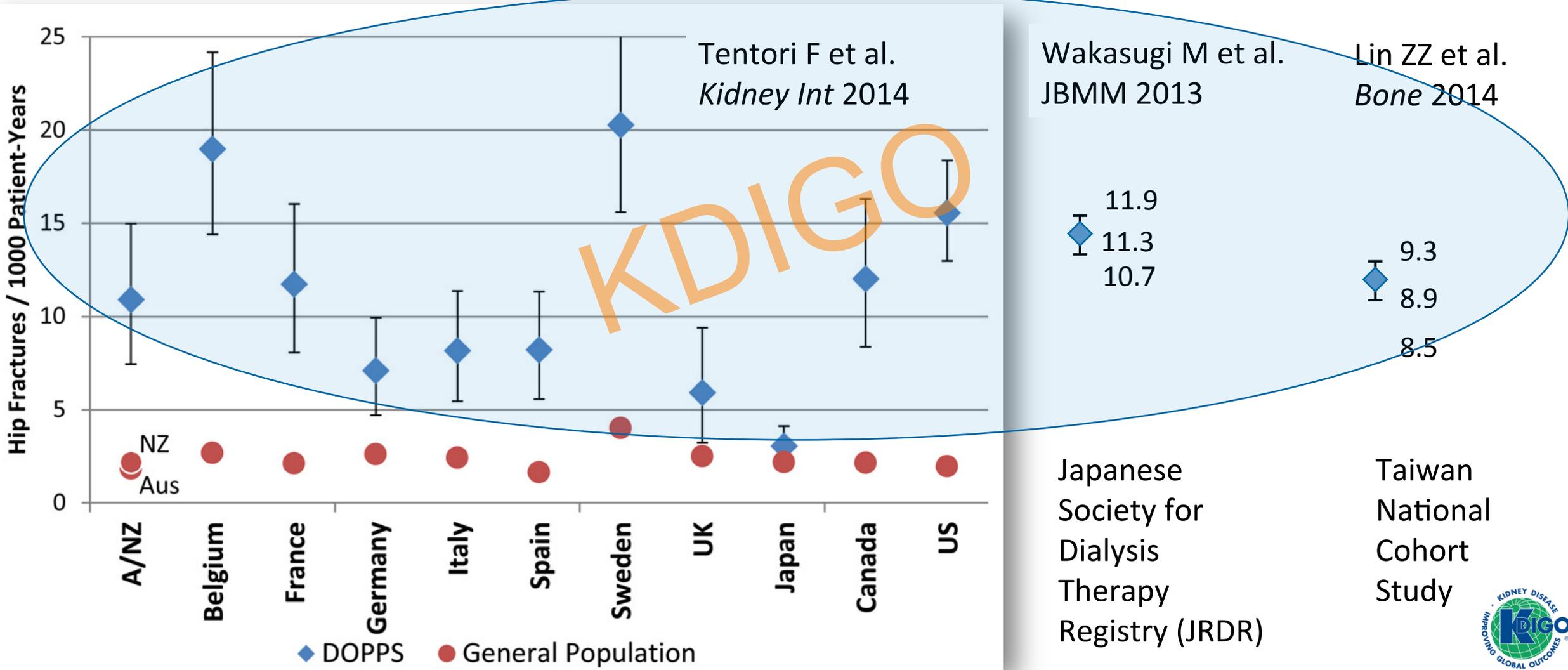
1903/*Patient time at risk* =
89.21/10,000

95% CI
= 85.2 to 93.3/10,000

Patient time at risk = 213316.9

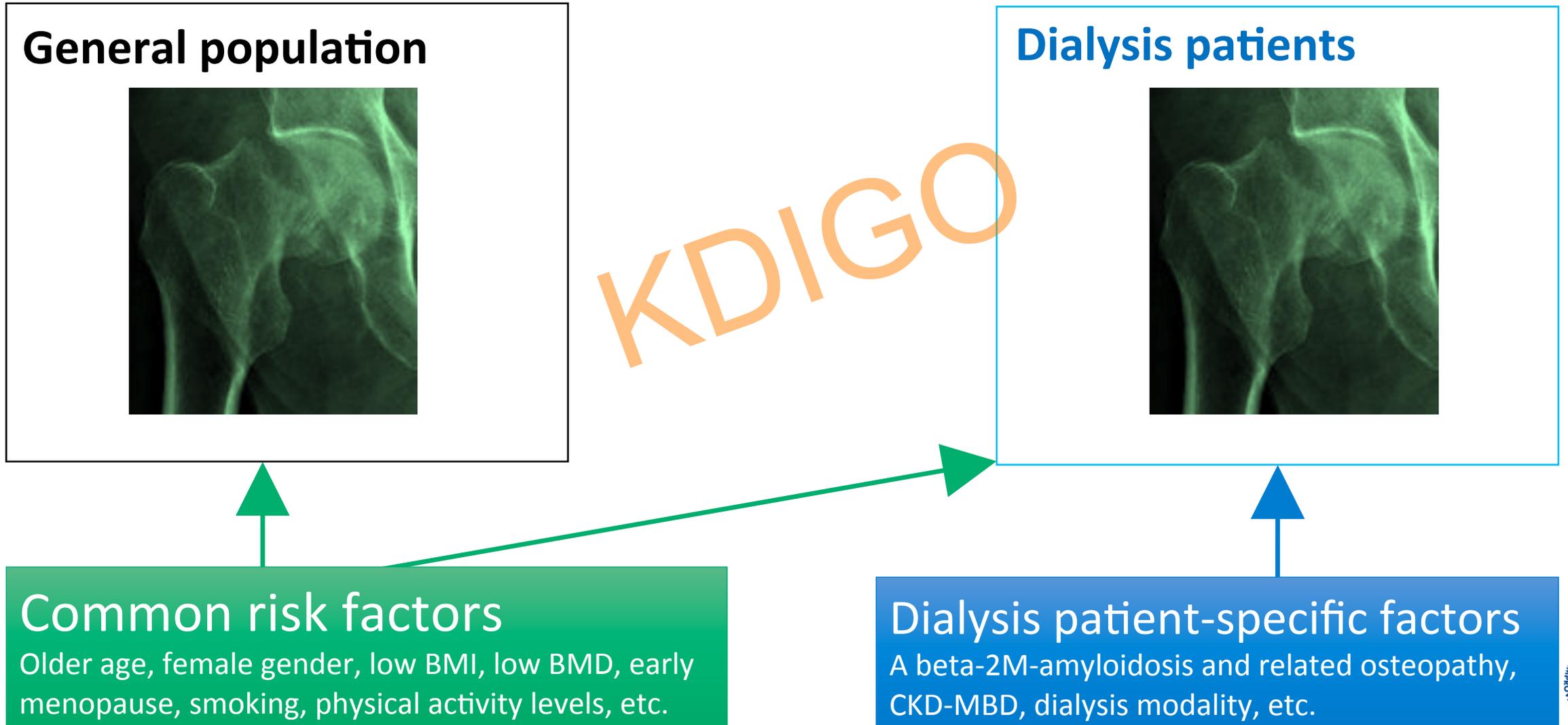


THE QUESTION ARISES WHY HIP FRACTURE INCIDENCE VARIES SO MUCH



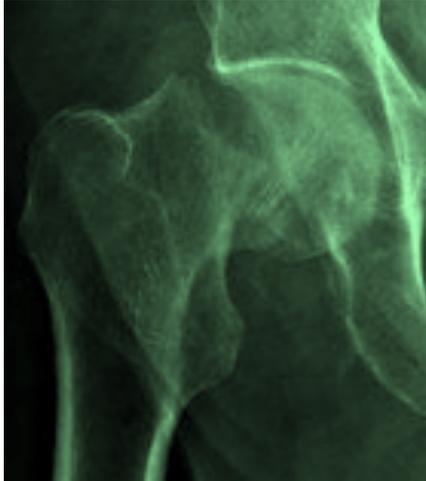
THE QUESTION ARISES WHY HIP FRACTURE INCIDENCE VARIES SO MUCH

THE REASONS ARE NOT KNOWN



LARGE VARIATIONS IN FRACTURE INCIDENCE EXIST IN THE GENERAL POPULATION

General population

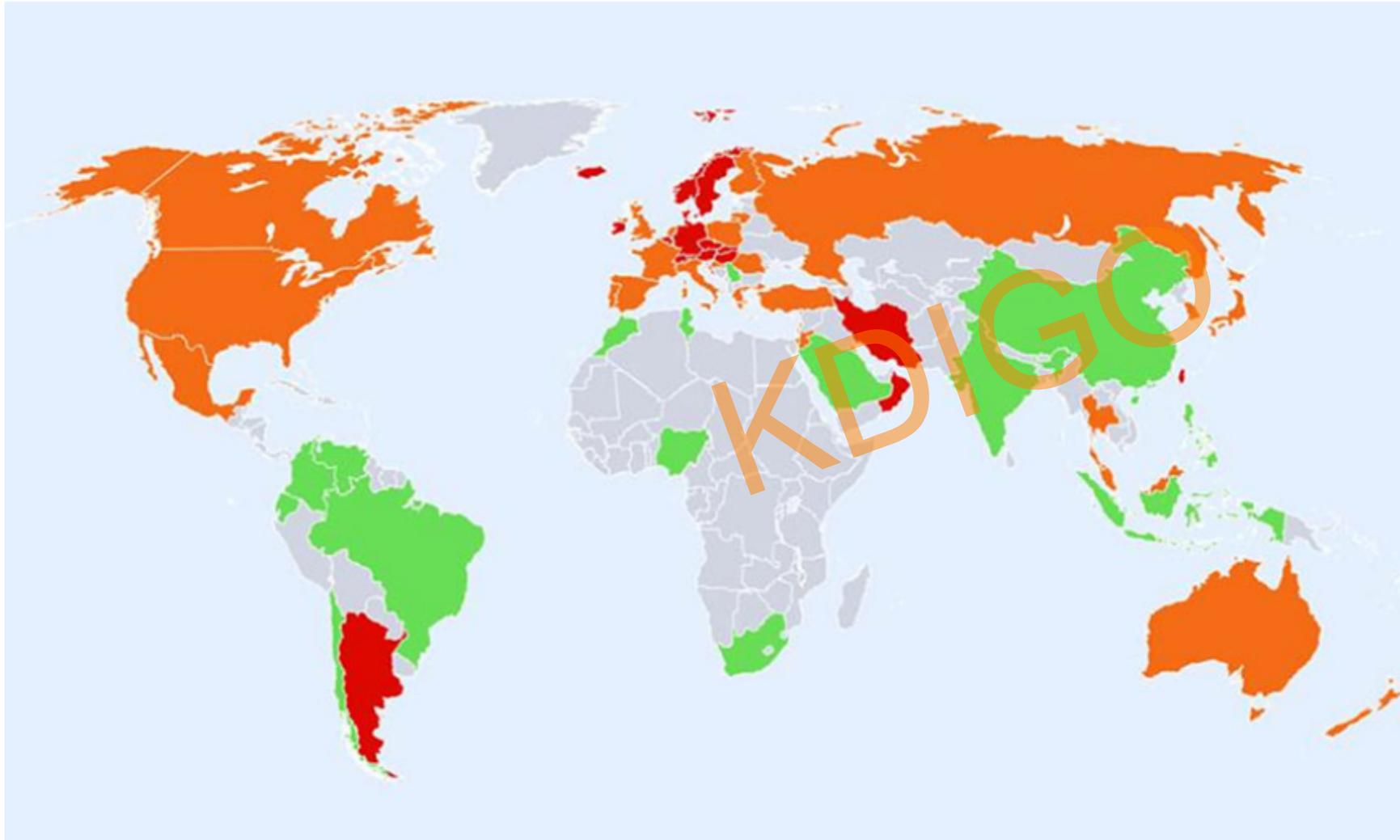


KDIGO

Common risk factors

Older age, female gender, low BMI, low BMD, early menopause, smoking, physical activity levels, etc.

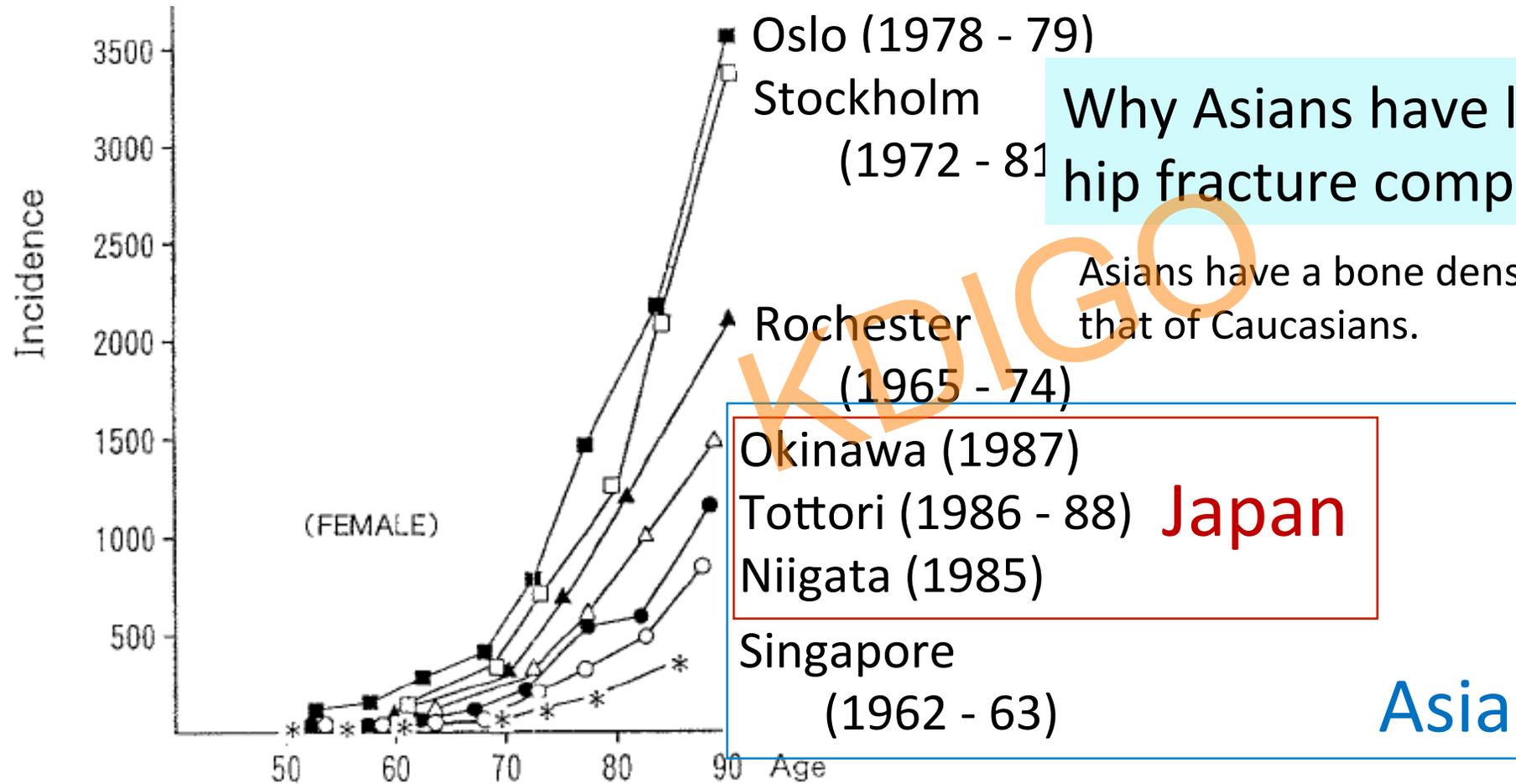
AGE-STANDARDIZED INCIDENCE RATES OF HIP FRACTURE VARIES ABOUT 10-FOLD IN THE GENERAL POPULATION



Hip fracture rates for men and women combined in different countries of the world categorised by risk.

Where estimates are available, countries are colour coded red (annual incidence >250/100,000), orange (150-250/100,000) or green (<150/100,000)

HIP FRACTURE INCIDENCE AMONG ASIANS ARE APPROXIMATELY HALF THAT OF CAUCASIANS FOR BOTH SEXES



Why Asians have lower incidence of hip fracture compared to Caucasians?

Asians have a bone density similar to or lower than that of Caucasians.

Okinawa (1987)
 Tottori (1986 - 88) **Japan**
 Niigata (1985)
 Singapore
 (1962 - 63)

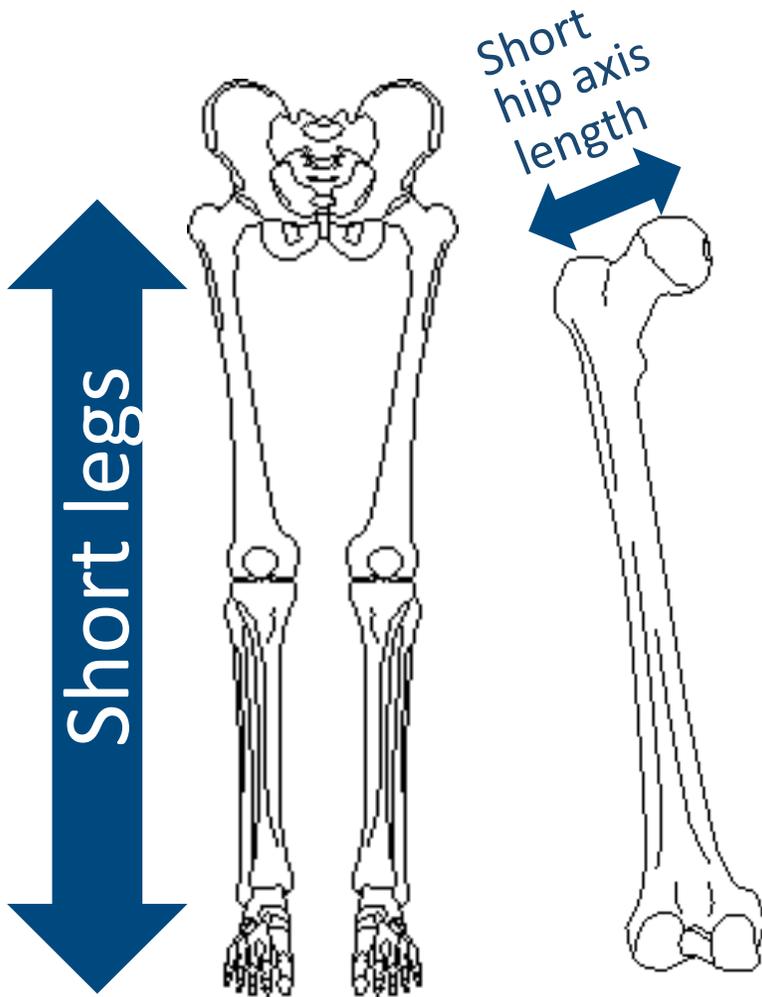
Asia

Fig. 1. Age-specific incidence of proximal femoral fractures in women in different countries.



THE REASONS WHY ASIANS HAVE LOWER INCIDENCE OF HIP FRACTURE COMPARED TO CAUCASIANS ARE NOT WELL UNDERSTOOD

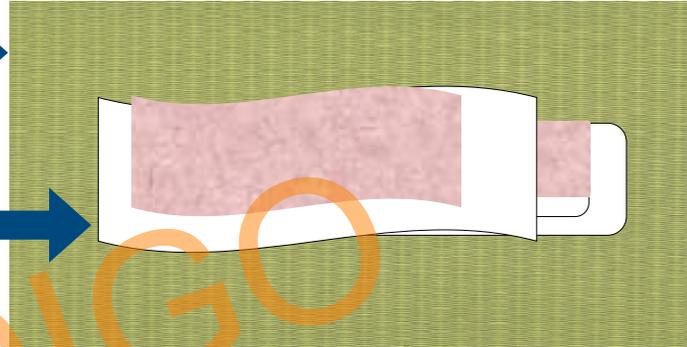
Some traditional lifestyle characteristics may prevent hip fracture.



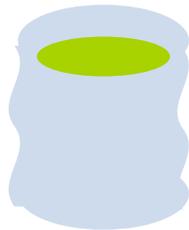
Tatami
(traditional Japanese mat)

Futon
bedding

The custom of living and sleeping on the floor on a *tatami*, and using *futon bedding*.



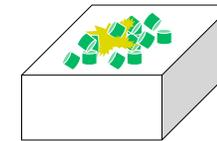
Japanese-style toilets
(squatting pan toilet)



Japanese
green tea

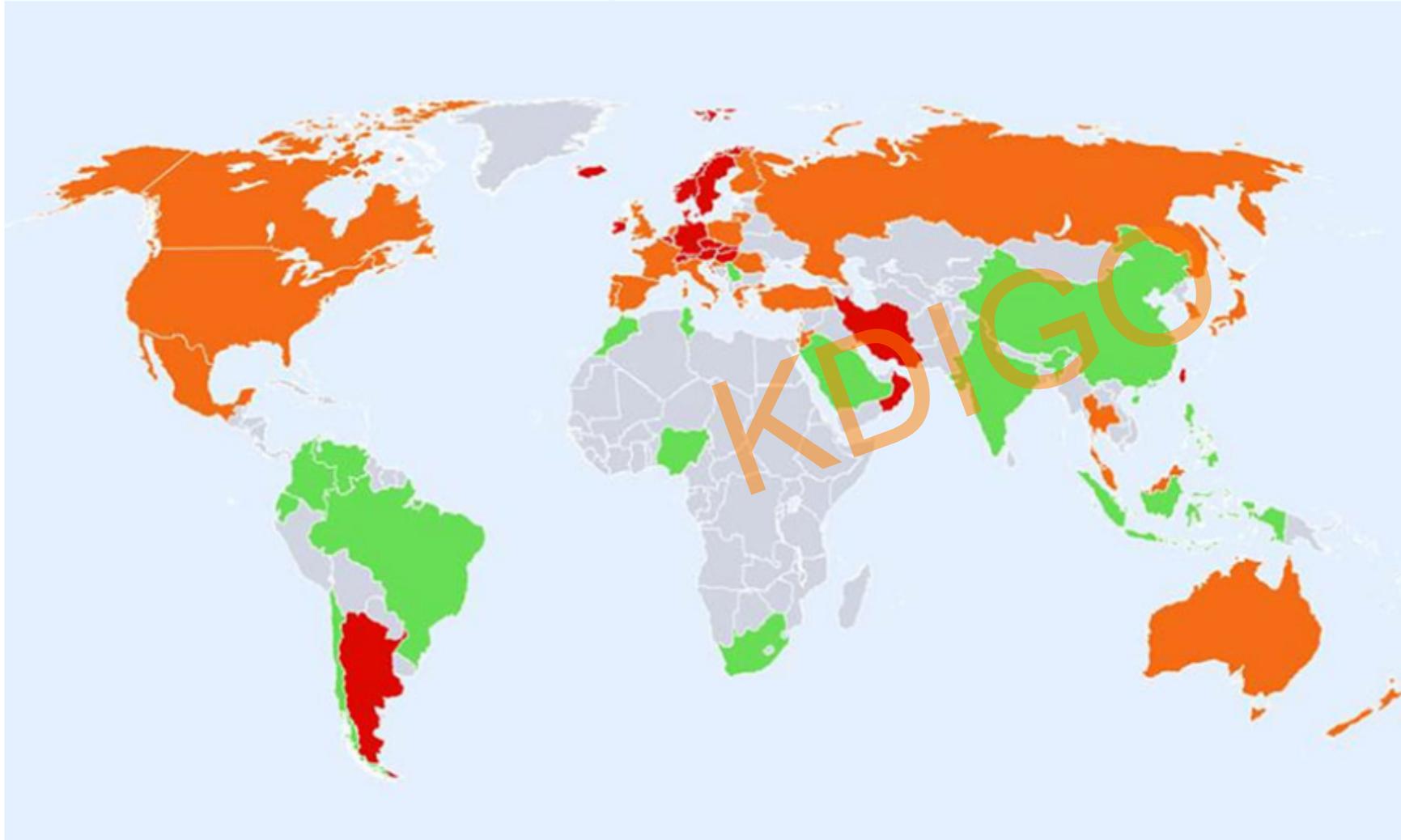


natto
fermented soybeans
rich in vitamin K₂
(menaquinone-7)



tofu
soy products containing
a high amount of isoflavones

IN ADDITION TO LARGE VARIATIONS IN FRACTURE RATES AROUND THE WORLD,



Hip fracture rates for men and women combined in different countries of the world categorised by risk.

Where estimates are available, countries are colour coded red (annual incidence >250/100,000), orange (150-250/100,000) or green (<150/100,000)

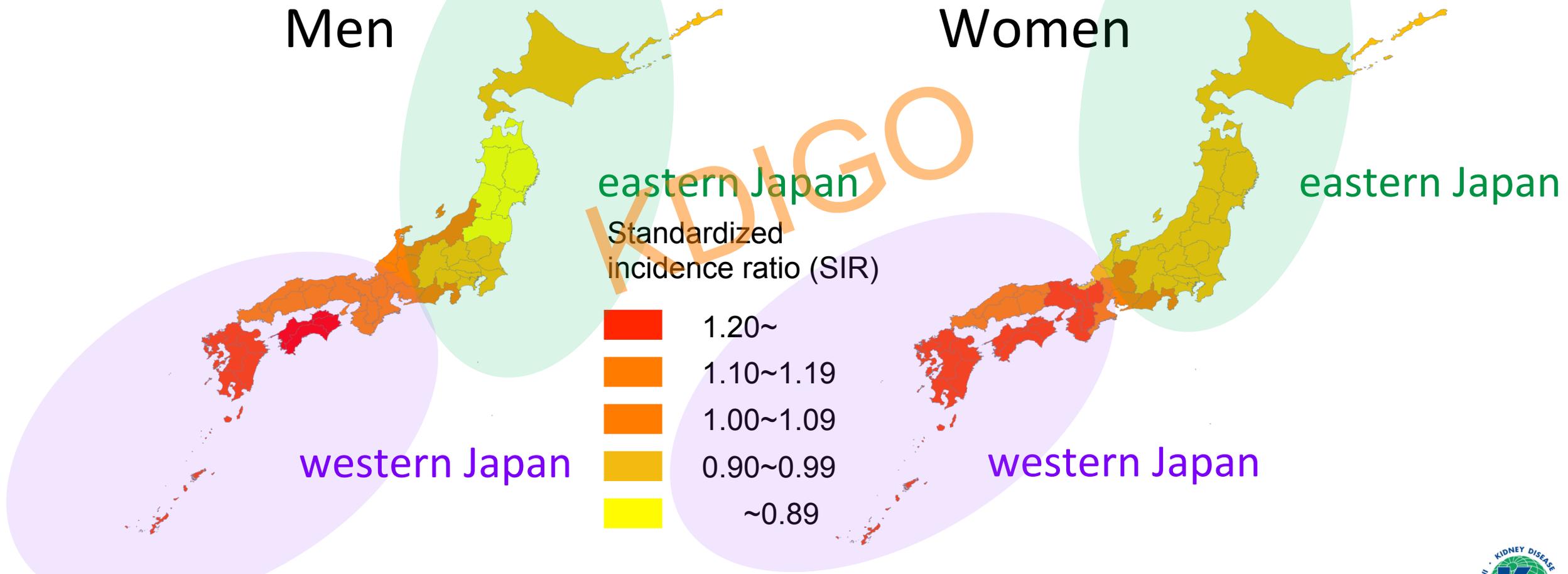
HIP FRACTURE RATES VARY WITHIN COUNTRIES

JAPANESE GENERAL POPULATION

Created based upon data from Yaegashi Y et al. *Eur J Epidemiol* 2008; 23:219-25

Men

Women

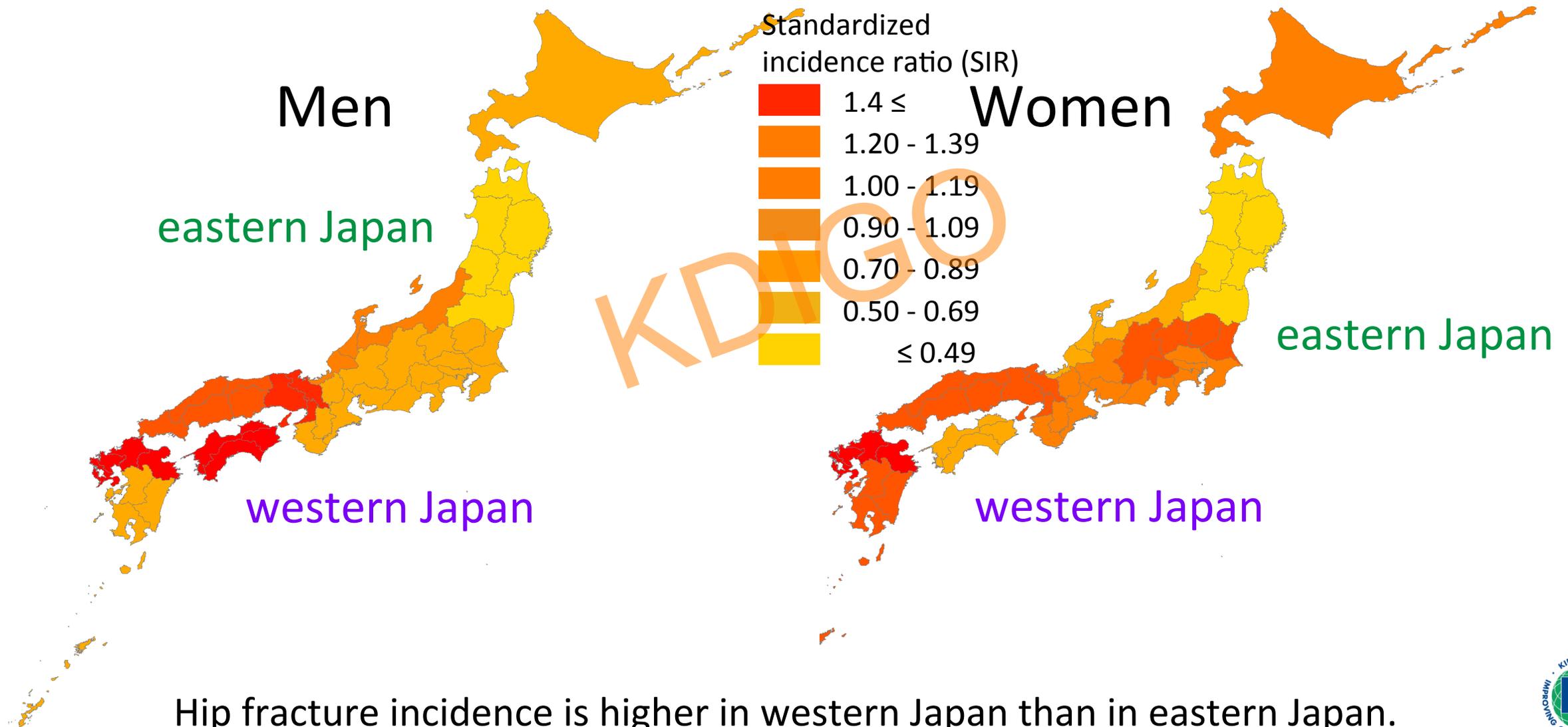


Hip fracture incidence is higher in western Japan than in eastern Japan.

HIP FRACTURE RATES VARY WITHIN COUNTRIES

JAPANESE HD PATIENTS

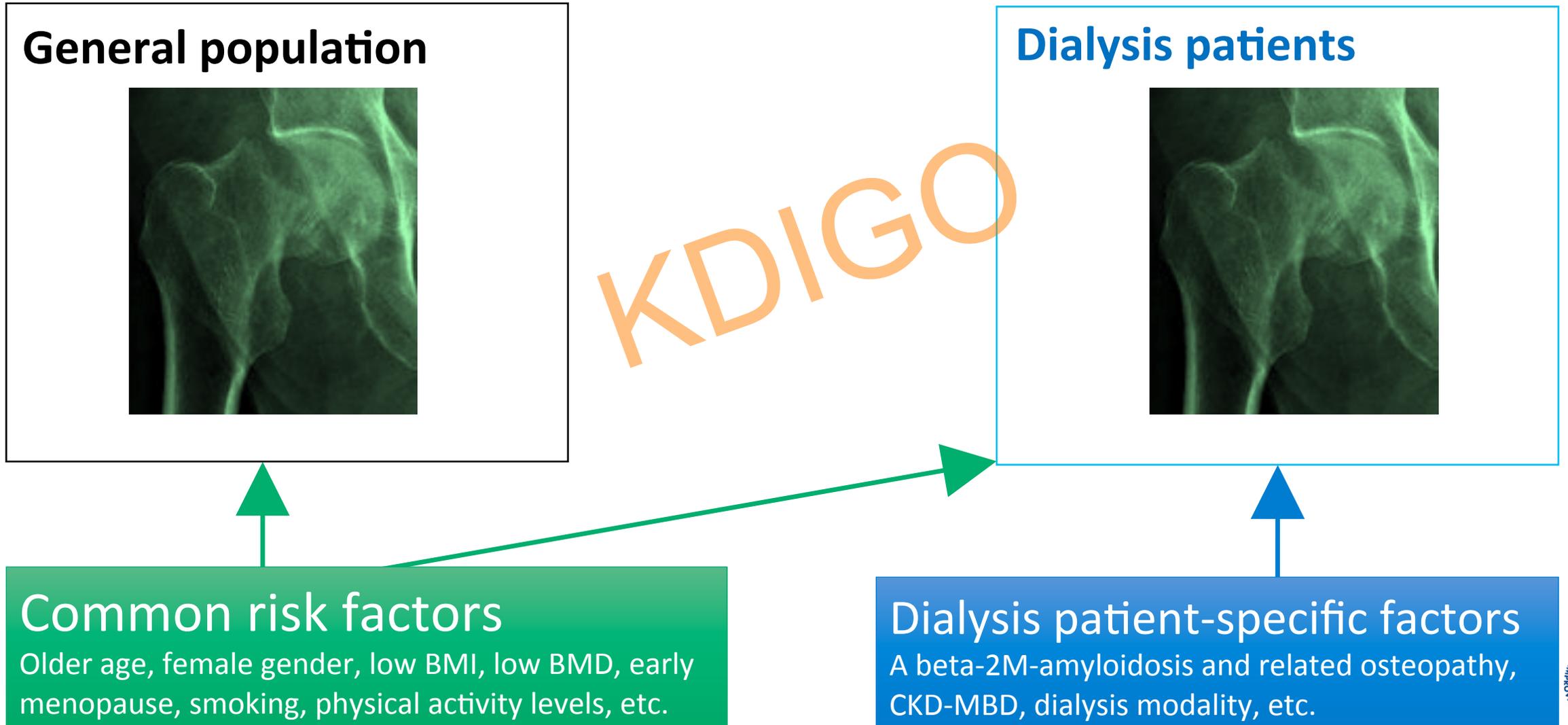
Wakasugi M, et al. *Ther Apher Dial* 2014;18:162-6.



Hip fracture incidence is higher in western Japan than in eastern Japan.

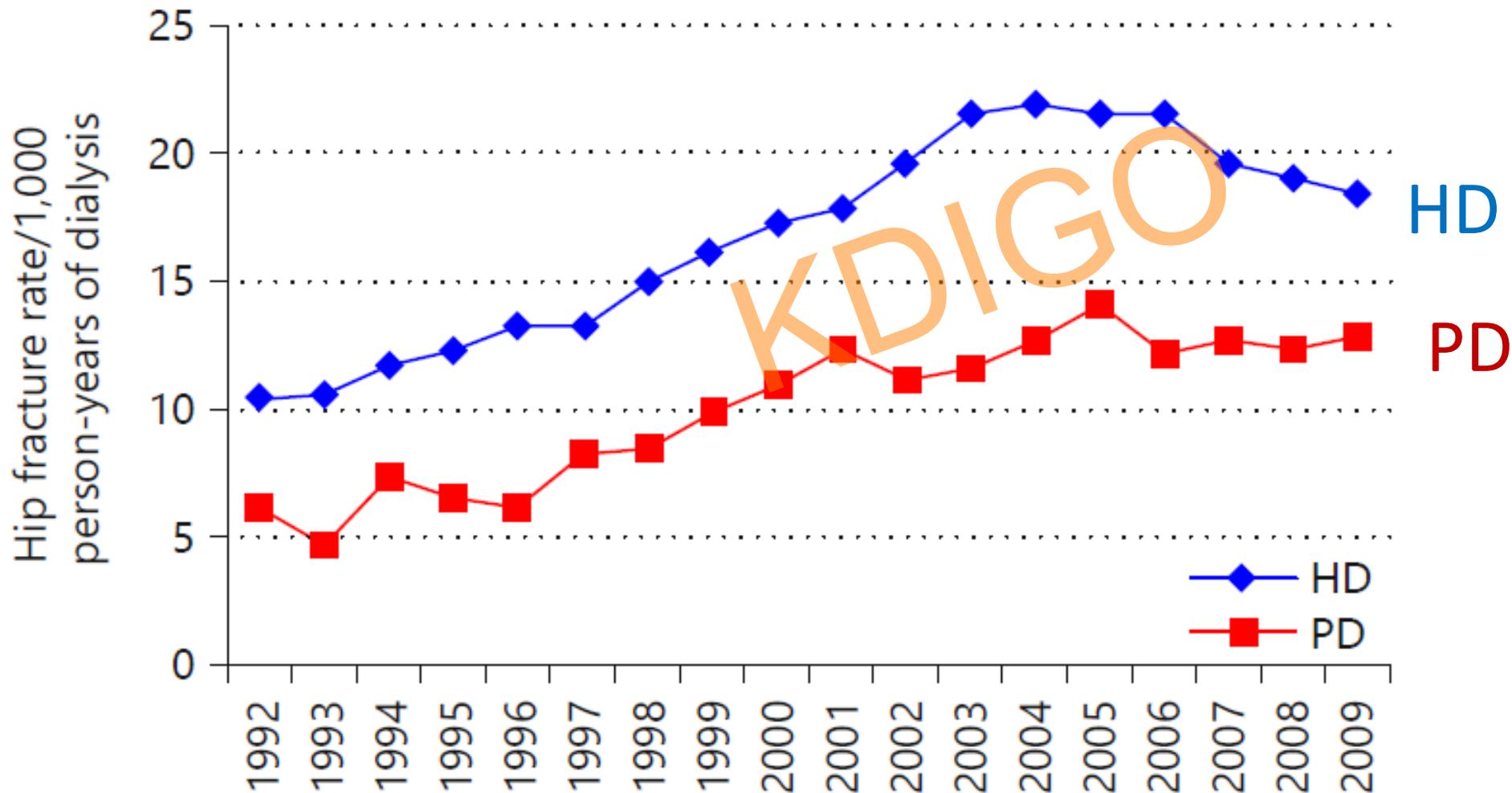
THE QUESTION ARISES WHY HIP FRACTURE INCIDENCE VARIES SO MUCH

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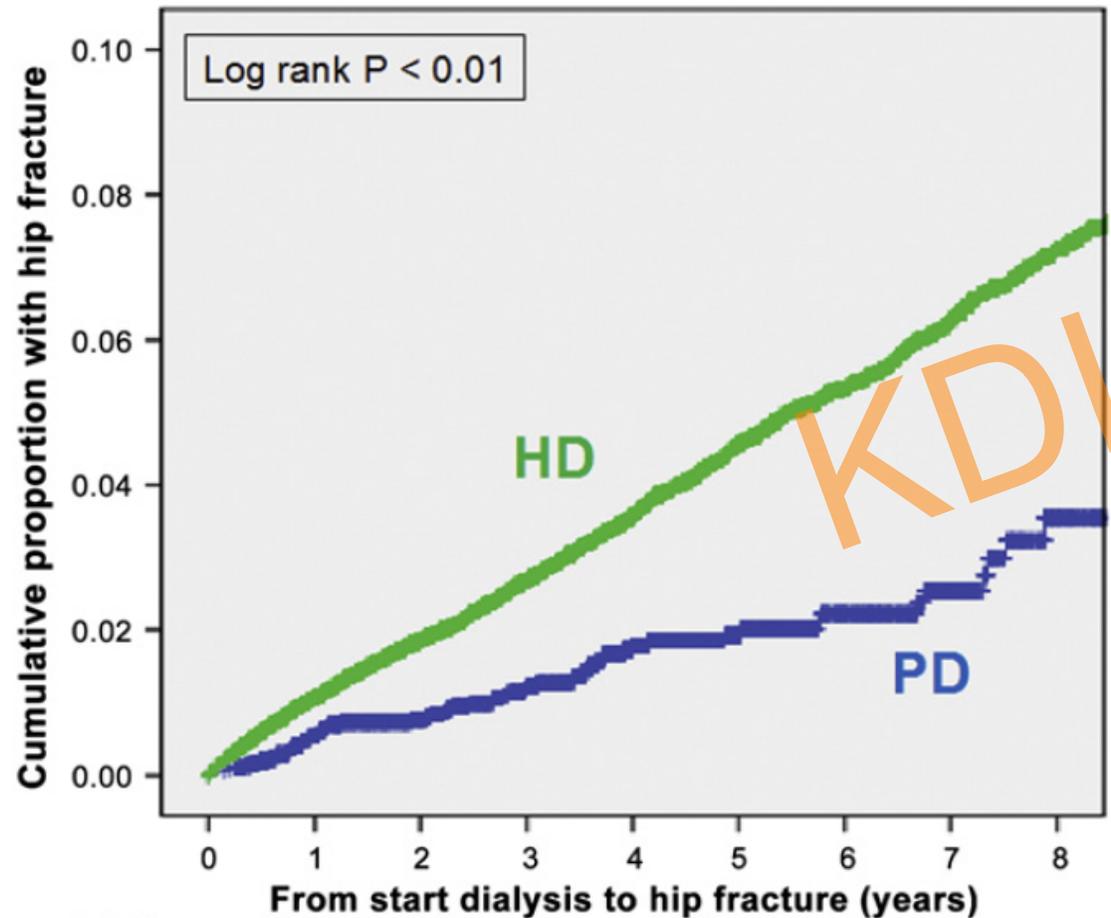
UNADJUSTED TEMPORAL TREND IN INCIDENCE OF HIP FRACTURES OVER TIME: HD COMPARED TO PD

Mathew AT, et al. *Am J Nephrol* 2014;40:451–457



CUMULATIVE INCIDENCE OF HIP FRACTURE AFTER BEGINNING DIALYSIS STRATIFIED BY DIALYSIS MODALITY

Lin ZZ, et al. *Bone* 2014;64:235–239



Number at risk

	0	1	2	3	4	5	6	7	8
HD	47986	42336	36459	31414	23086	16398	11299	7265	4092
PD	3487	3155	2750	2369	1684	1219	829	527	282

Table 2

Risk factor for hip fracture in patients with end-stage renal disease and on dialysis (n = 51,473).

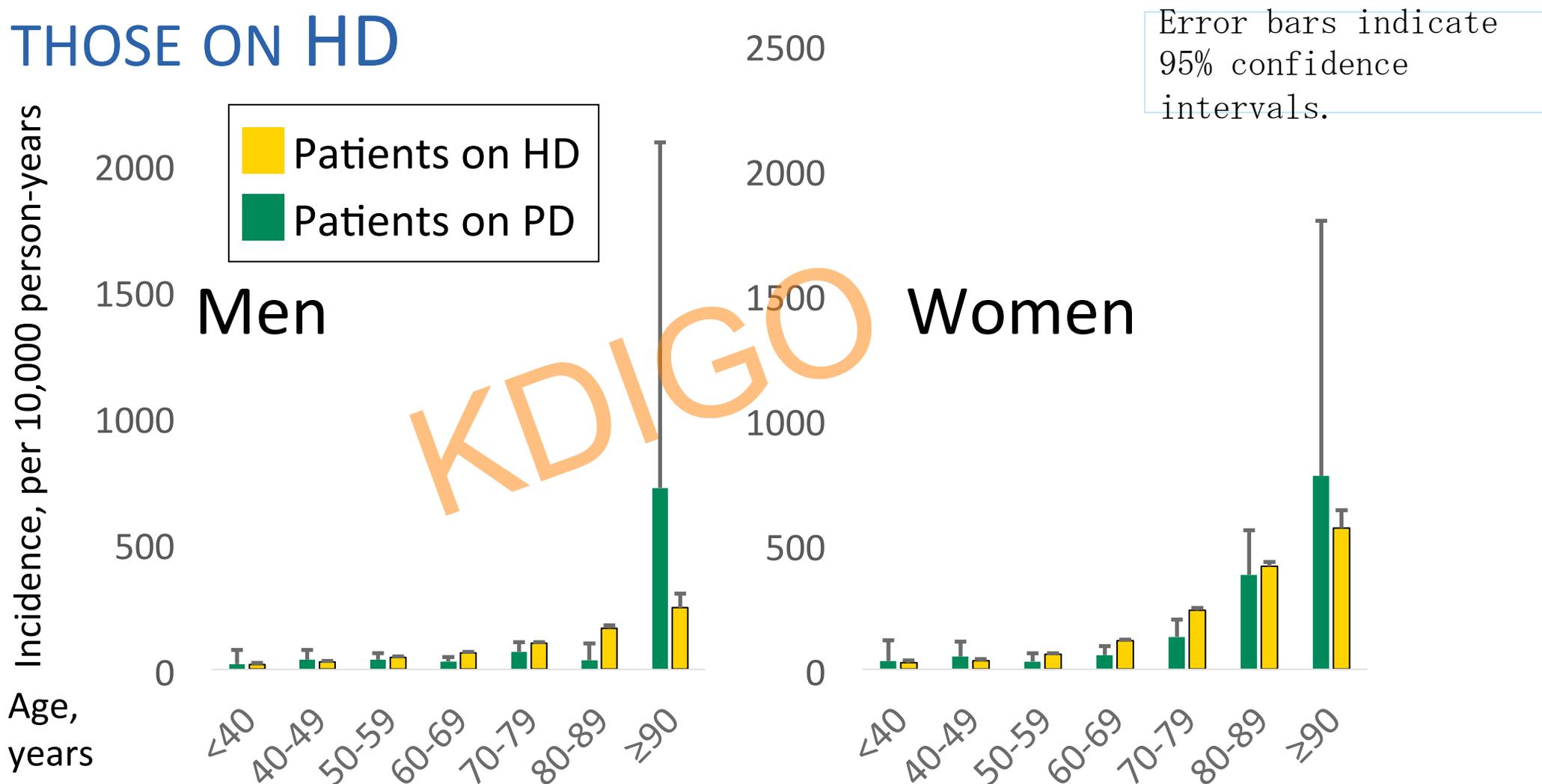
Factors	Univariate analysis	Multivariate analysis
	HR (95% CI)	HR (95% CI) ^a
Sex (female v male)	1.343 (1.225–1.473)*	1.256 (1.143–1.380)*
Age		
18–44	1	1
45–64	5.159 (3.820–6.967)*	4.269 (3.154–5.780)*
>65	17.085 (12.721–22.947)*	13.649 (10.124–18.401)*
Dialysis modality (HD v PD)	2.269 (1.755–2.934)*	1.311 (1.012–1.698)*
Prior transplantation (yes v no)	0.300 (0.113–0.801)	1.094 (0.408–2.930)
Prior hip fracture (yes v no)	2.718 (2.182–3.385)*	1.438 (1.149–1.798)*
Osteoporosis (yes v no)	1.894 (1.633–2.197)*	1.242 (1.066–1.448)*
Diabetic Mellitus (yes v no)	2.001 (1.825–2.195)*	1.662 (1.511–1.828)*
Congestive heart failure (yes v no)	1.532 (1.386–1.694)*	1.099 (0.992–1.218)
Cerebrovascular disease (yes v no)	1.654 (1.455–1.879)*	1.149 (0.804–1.642)
Liver cirrhosis (yes v no)	1.276 (1.067–1.526)*	1.374 (1.149–1.644)*
Psychiatric disorder (yes v no)	1.240 (0.865–1.779)	1.201 (0.837–1.725)
Dementia (yes v no)	1.617 (0.868–3.012)	0.853 (0.457–1.593)

HR, hazard ratio; CI, confidence interval; HD, hemodialysis; PD, peritoneal dialysis.

^a HR adjusted for sex, age, dialysis modalities, prior transplantation, prior hip fracture, osteoporosis, diabetes mellitus, congestive heart failure, cerebrovascular accident, liver cirrhosis, psychiatric disorder and dementia.

* p < 0.05.

PATIENTS ON PD HAD ABOUT 30% LOWER RISK OF HIP FRACTURE THAN DID THOSE ON HD



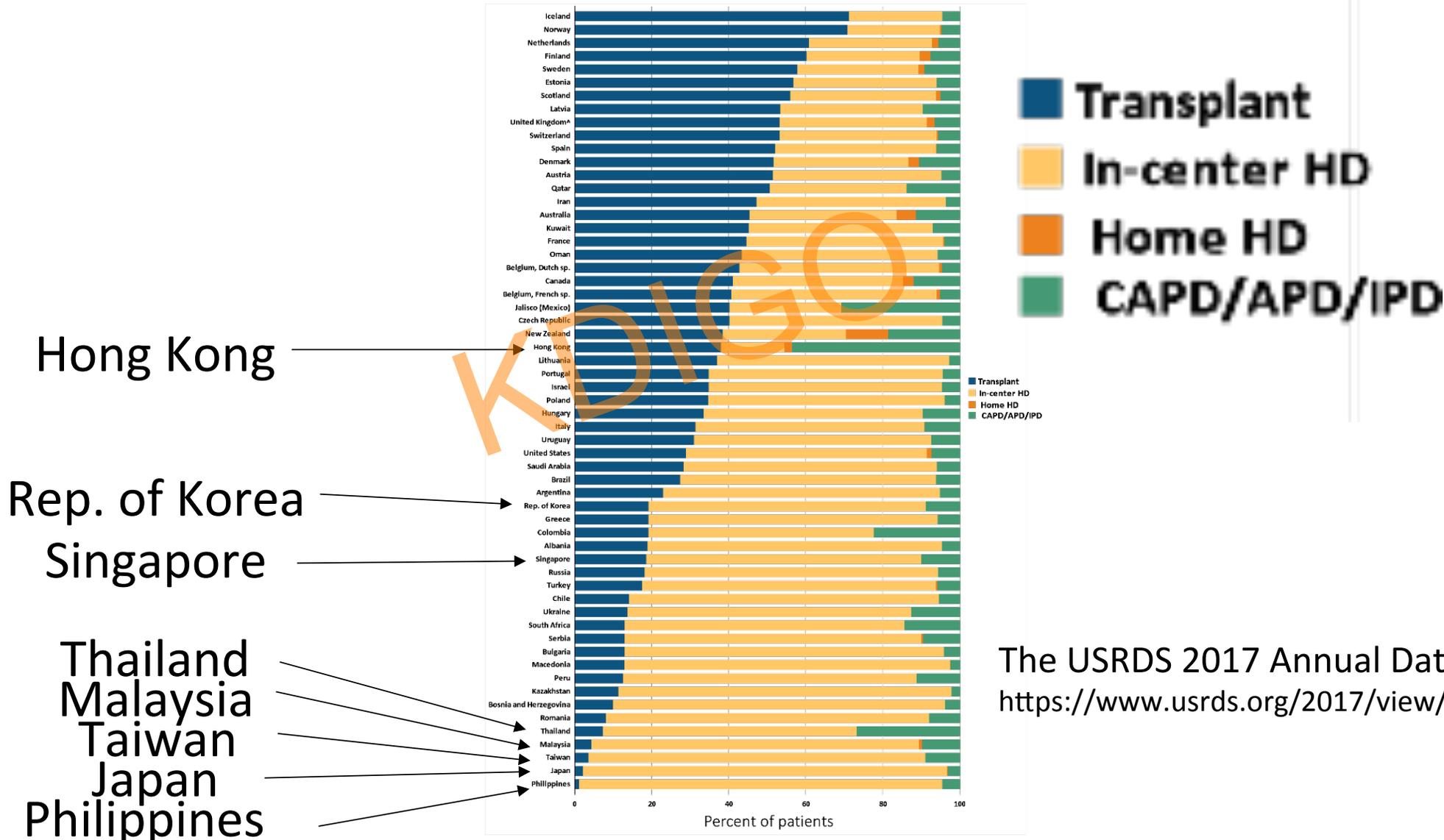
SIR 0.64 (95%CI 0.49 – 0.81)

0.69 (95%CI 0.55 – 0.85)

Calculated using data from Tables S3-S5 in Wakasugi M, et al. *Am J Kidney Dis.* 2018;71:173-181.



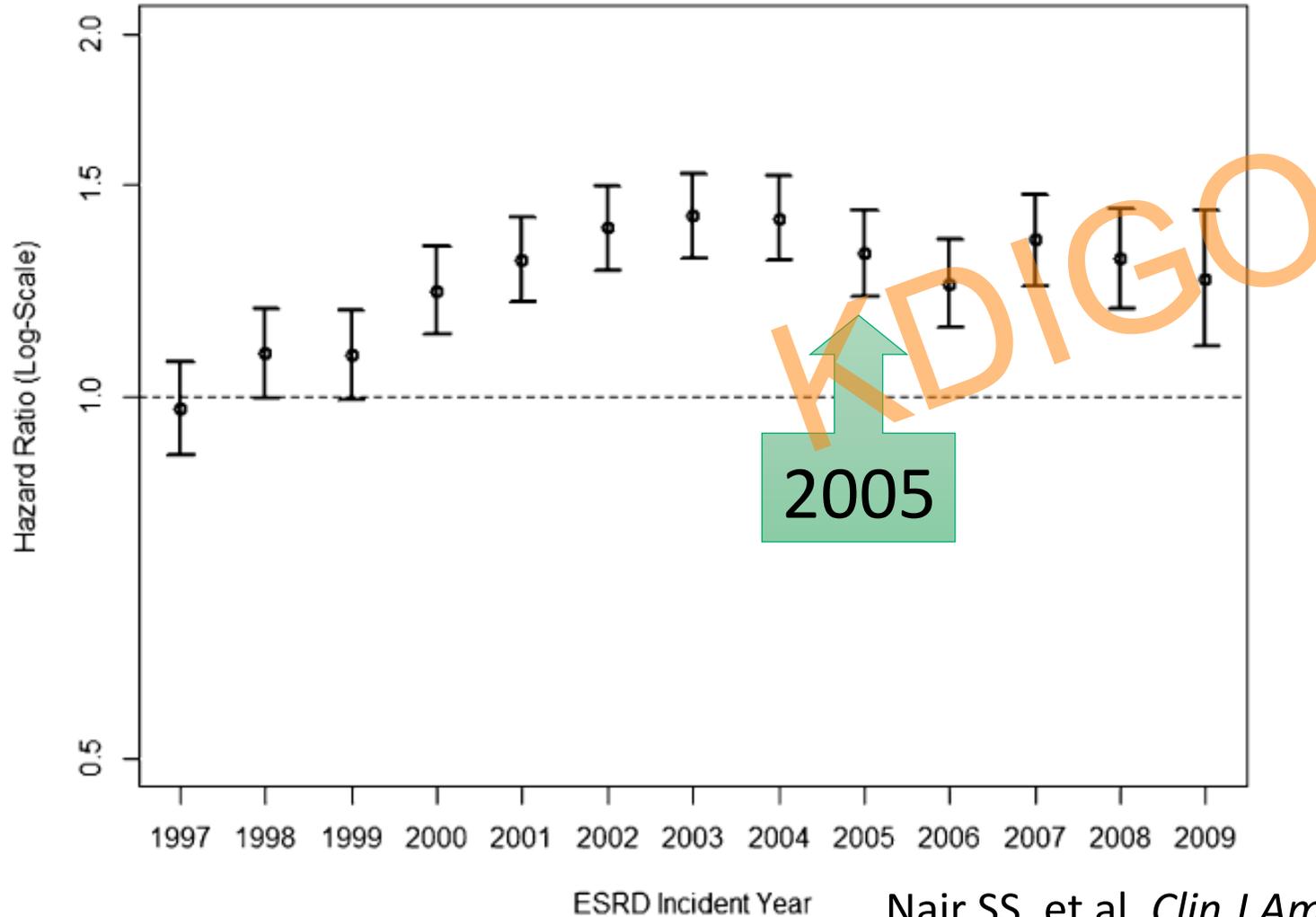
FIGURE 11.12 PERCENTAGE DISTRIBUTION OF TYPE OF RENAL REPLACEMENT THERAPY MODALITY USED BY ESRD PATIENTS, BY COUNTRY, IN 2015



The USRDS 2017 Annual Data Report
<https://www.usrds.org/2017/view/Default.aspx>



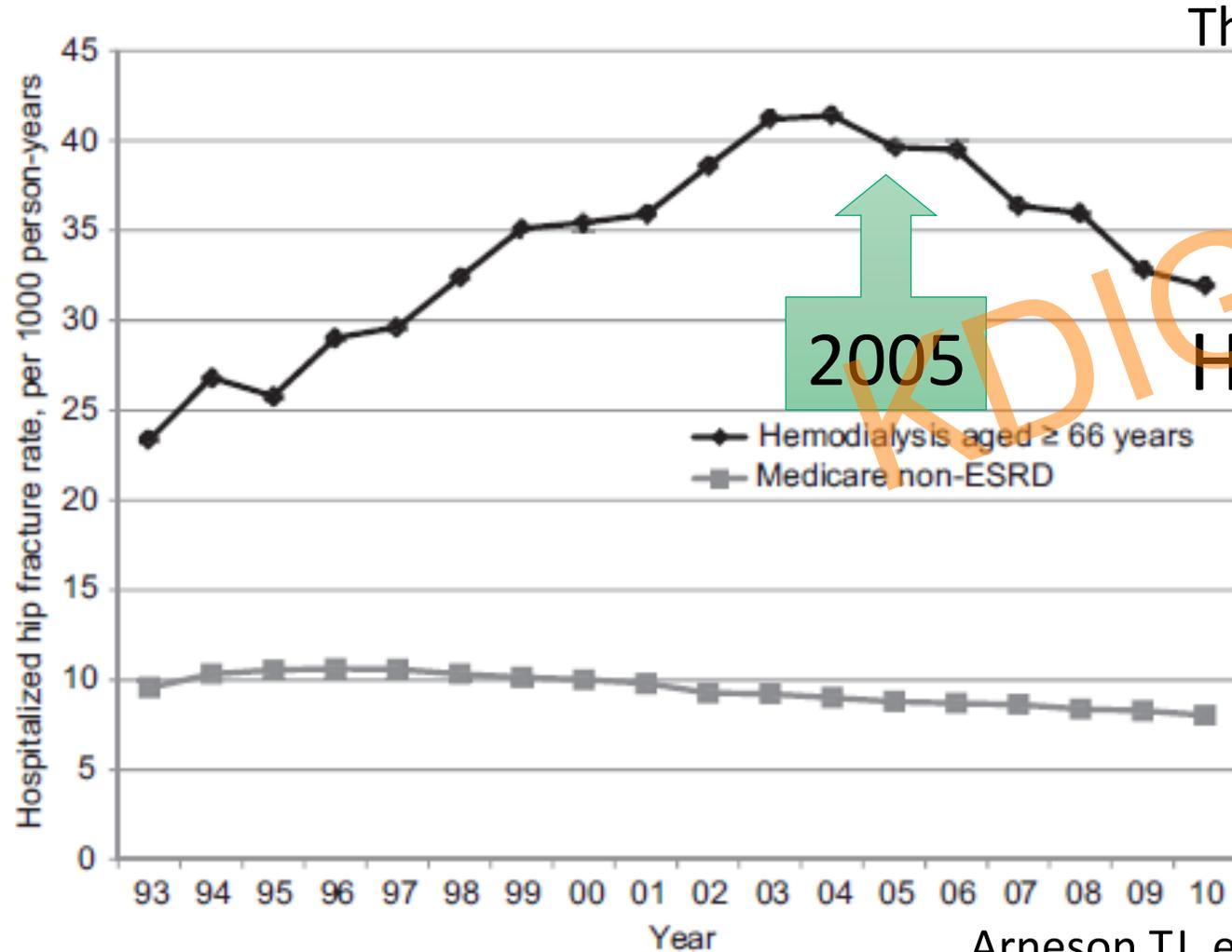
INCIDENCE RATES FOR HIP FRACTURE HAVE DECLINED SINCE 2005 AMONG INCIDENT DIALYSIS PATIENTS IN THE US



ESRD Incident Year

Nair SS, et al. *Clin J Am Soc Nephrol* 2013; 8: 1336–42.

TRENDS ARE DIFFERENT BETWEEN THE GENERAL NON-ESRD POPULATION AND HD PATIENTS



The improved trend in the hemodialysis pts is suggested to be due to factors specific to hemodialysis pts.

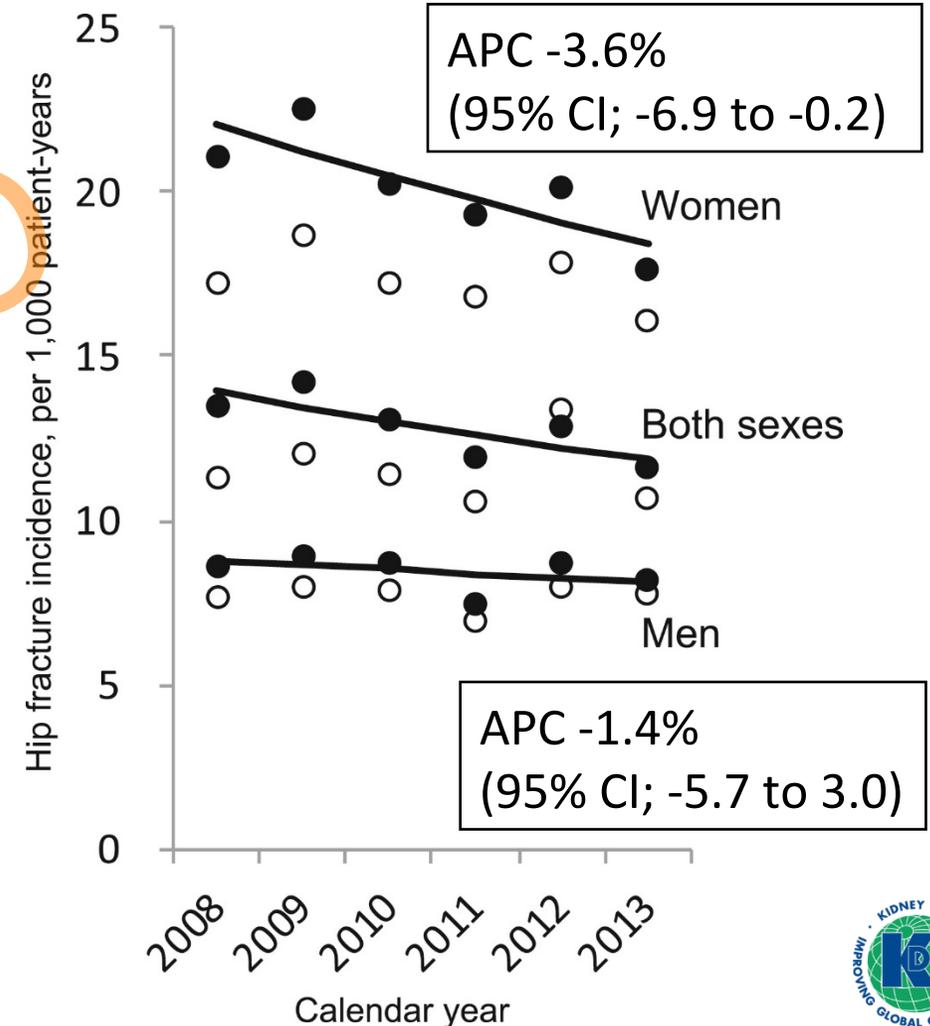
Hemodialysis aged \geq 66years

Medicare non-ESRD

AGE-STANDARDIZED HIP FRACTURE INCIDENCE IN JAPAN HAVE DECLINED IN FEMALE AND SHOWED NO CHANGE IN MALE DIALYSIS PATIENTS

Wakasugi M, et al. *Am J Kidney Dis.* 2018;71:173-181.

KDIGO

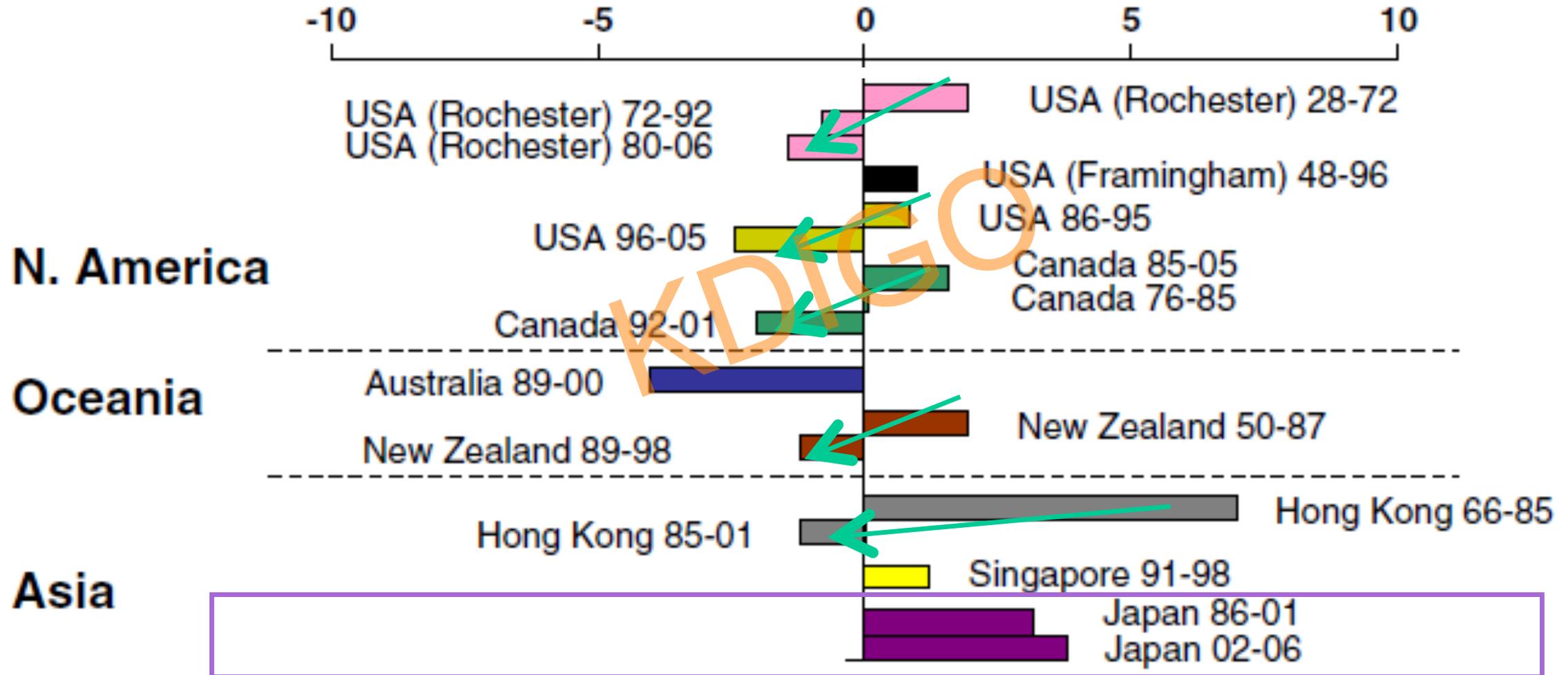


Open and filled circles represent the crude and age-standardized rates, respectively.

The reference population was the 2013 population of Japanese dialysis patients.

Lines are fitted rates based on joinpoint analysis.

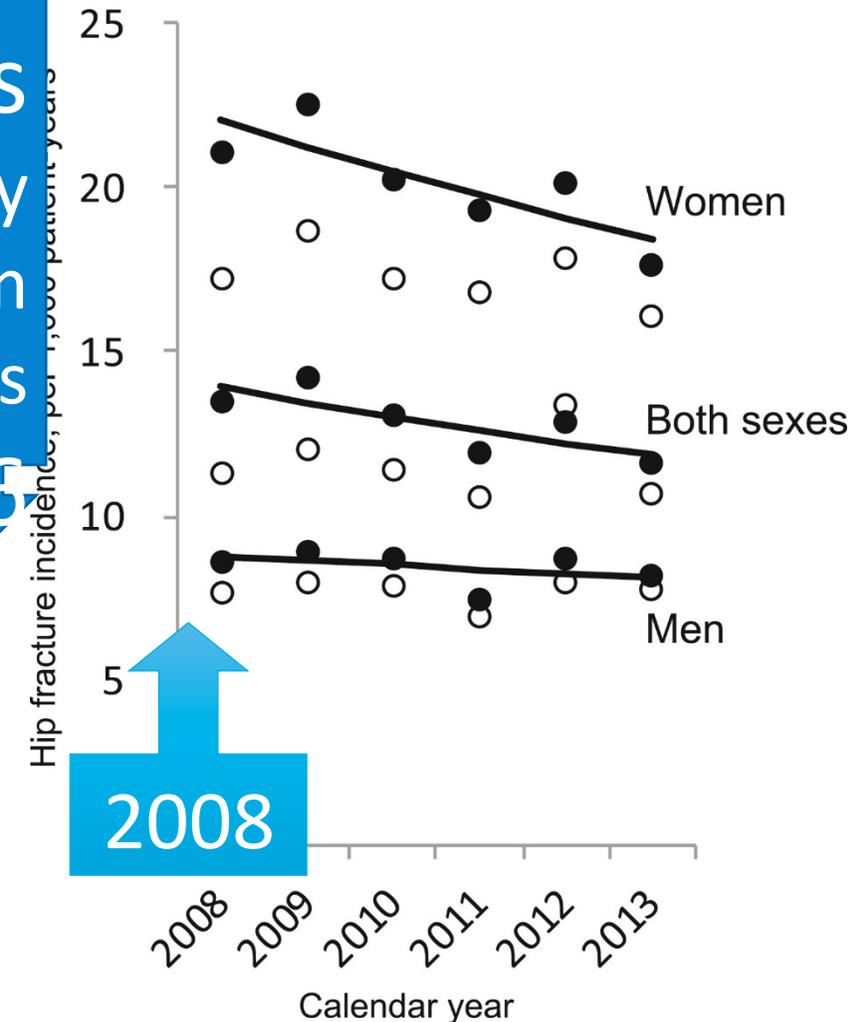
JAPANESE GENERAL POPULATION HAS A CONTINUING INCREASE IN AGE-ADJUSTED RATES OF HIP FRACTURE



EVIDENCE-BASED GUIDELINES AND THE CONCEPT OF CKD-MBD MAY CONTRIBUTE TO THE IMPROVEMENTS

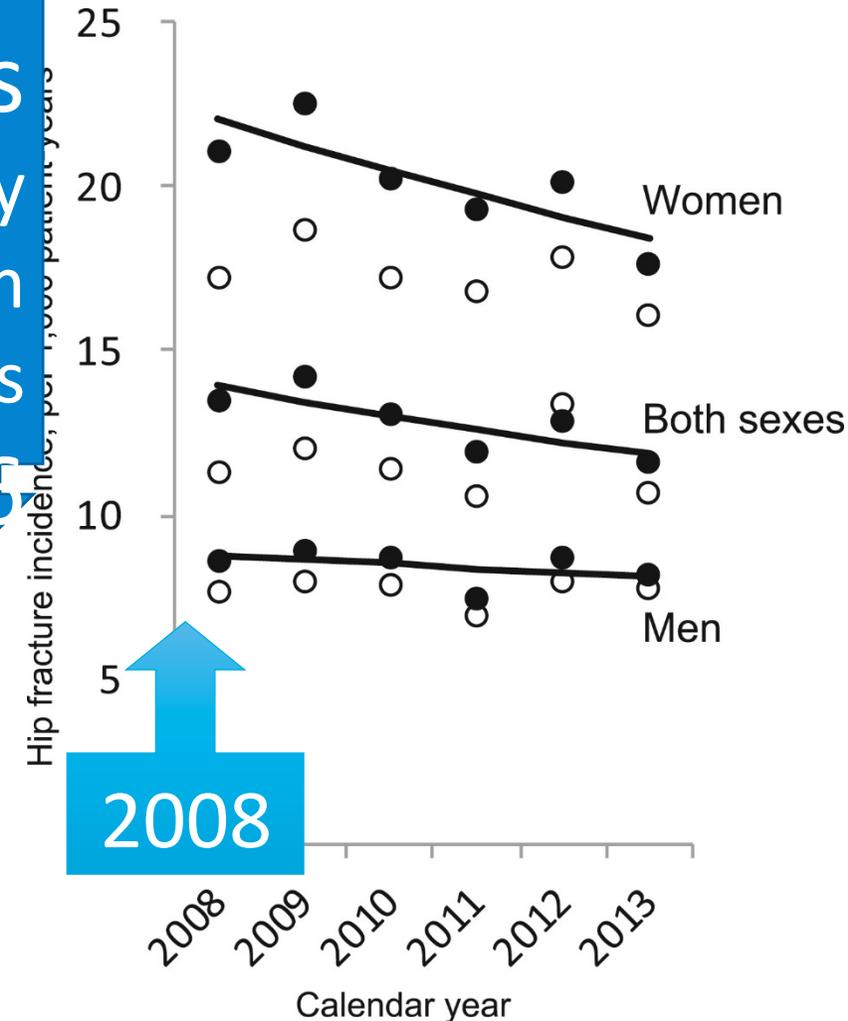
The JSDT clinical practice guidelines
for management of secondary
hyperparathyroidism
in maintenance dialysis patients

This is the first clinical guidelines to be published after
the clinical concept of CKD-MBD was introduced by KDIGO.



THE TARGET RANGE FOR INTACT PTH IS MUCH LOWER THAN THOSE FROM OTHER COUNTRIES

The JSDT clinical practice guidelines for management of secondary hyperparathyroidism in maintenance dialysis patients



Target range for dialysis patients

the JSDT clinical practice guideline in 2006

the JSDT clinical practice guideline in 2012

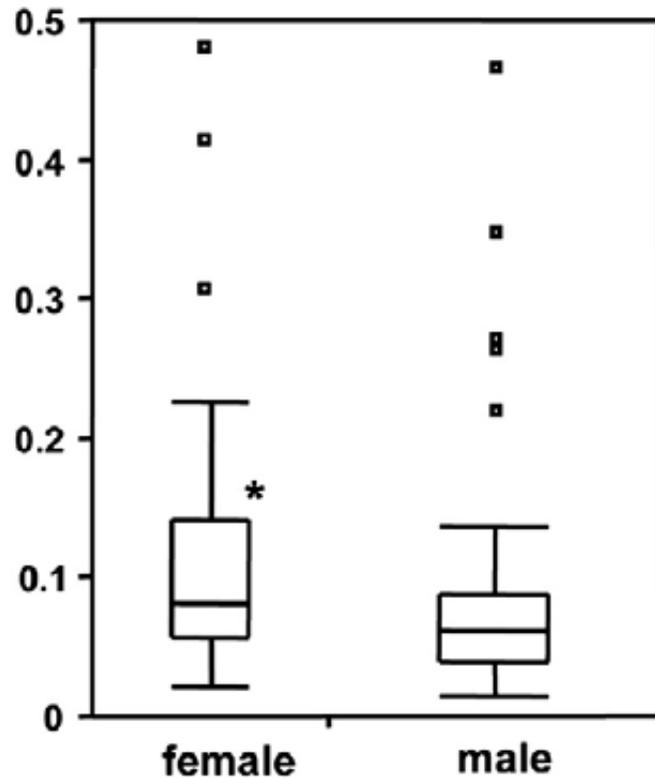
Intact PTH

60-180 pg/mL

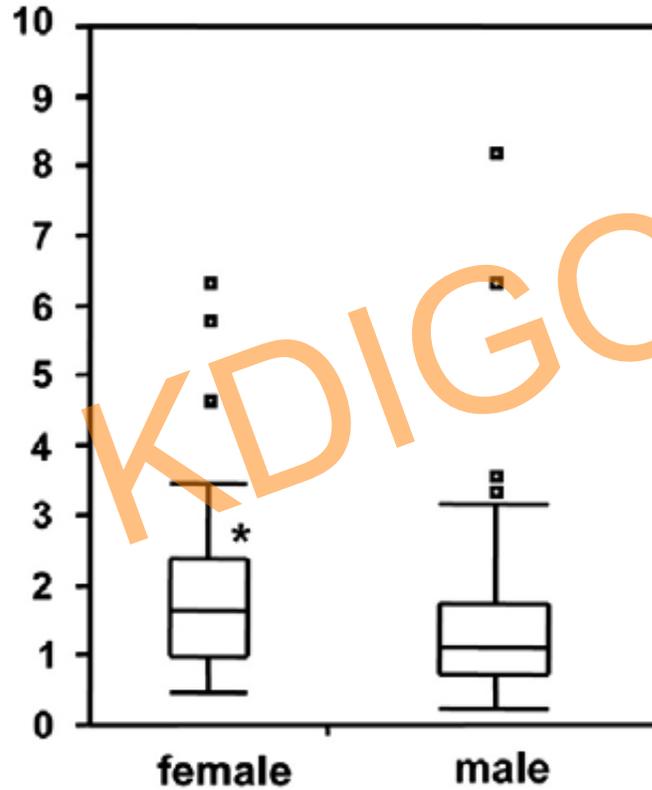
60-240 pg/mL

POSTMENOPAUSAL FEMALE DIALYSIS PATIENTS HAVE MORE BONE LOSS THAN MALE DIALYSIS PATIENTS WITH COMPARABLE PTH CONCENTRATIONS

TRAP5b/1-84 PTH



NTX/1-84 PTH



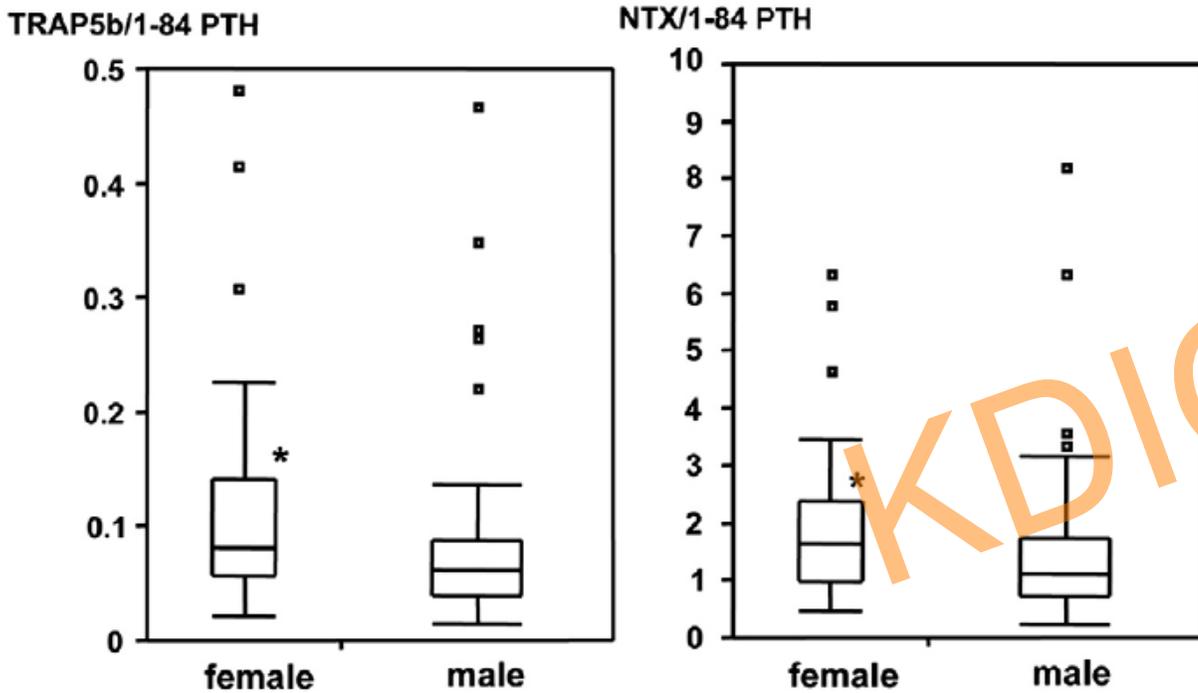
Hamano T, et al. *Bone*. 2009;45:S19-S25.

KDIGO

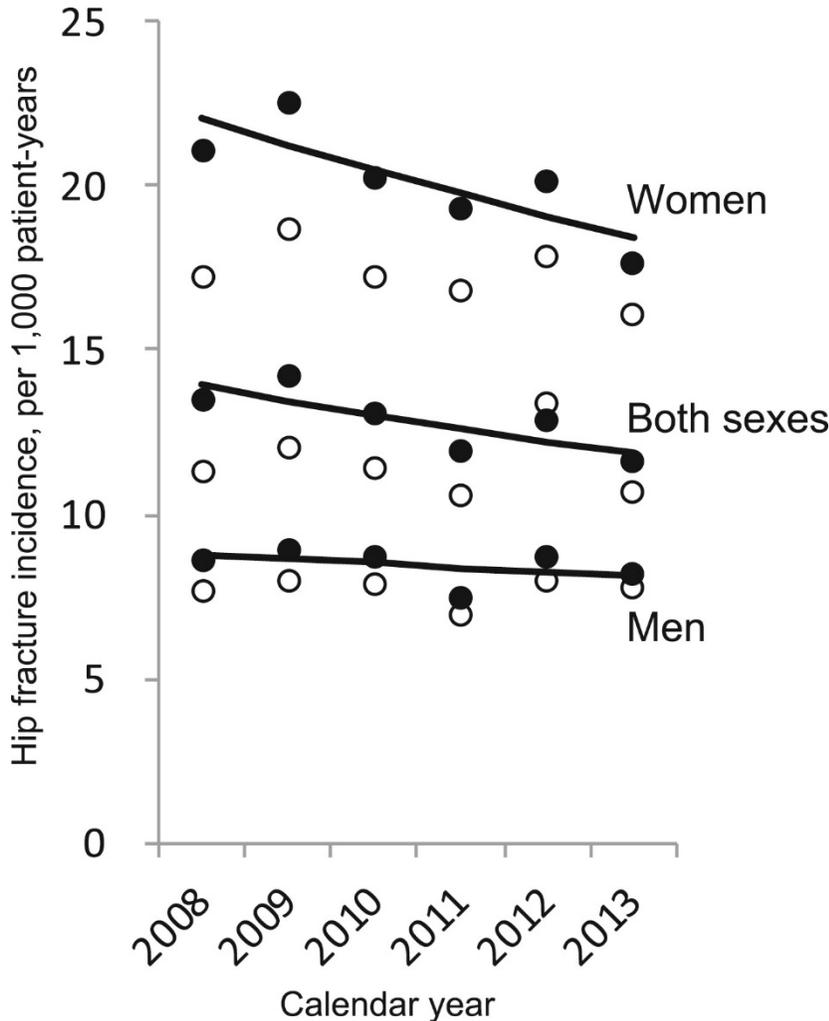
Concentrations of serum bone resorption markers are significantly higher in postmenopausal female hemodialysis patients compared with males with similar serum PTH concentrations.

THE TARGET RANGE IN JAPAN MAY BE FAVORABLE FOR FEMALE BONES

Hamano T, et al. *Bone*. 2009;45:S19-S25.



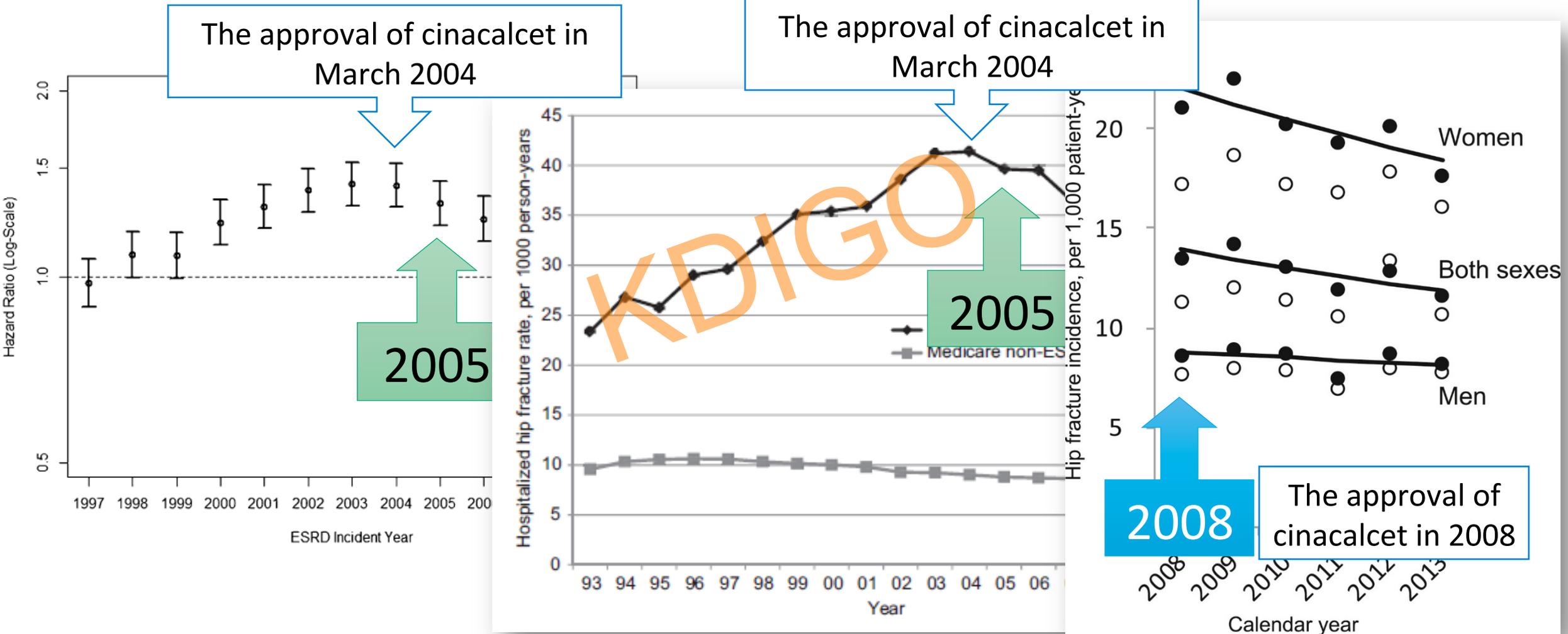
Wakasugi M, et al. *Am J Kidney Dis*. 2018;71:173-181.



Target range for dialysis patients	the JSDT clinical practice guideline in 2006	the JSDT clinical practice guideline in 2012
Intact PTH	60-180 pg/mL	60-240 pg/mL



THE IMPROVED TREND IN THE DIALYSIS PATIENT IS LIKELY DUE TO FACTORS SPECIFIC TO DIALYSIS PATIENTS.



Nair SS, et al. *Clin J Am Soc Nephrol* 2013; 8: 1336-42.

Arneson TJ, et al. *Am J Kidney Dis*. 2013; 62:747-754.

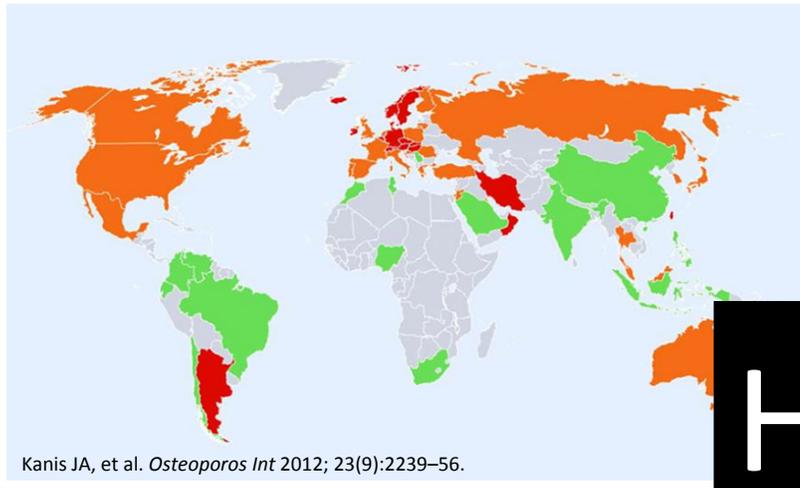
Wakasugi M, et al. *Am J Kidney Dis*. 2018;71:173-181.



SUMMARY

Poor outcome

General population



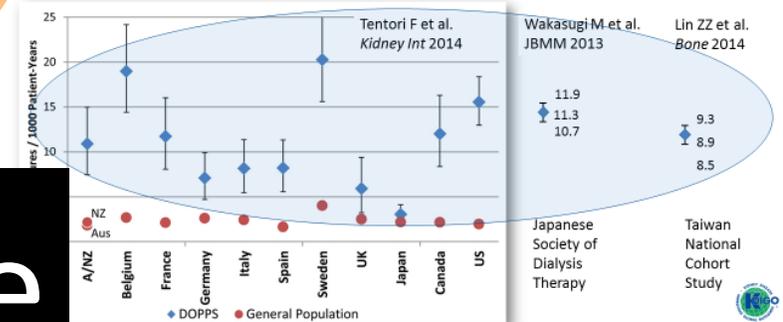
Hip fracture

Common risk factors

Older age, female gender, low BMI, low BMD, early menopause, smoking, physical activity levels, etc.

Dialysis patients

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THE REASONS ARE NOT KNOWN

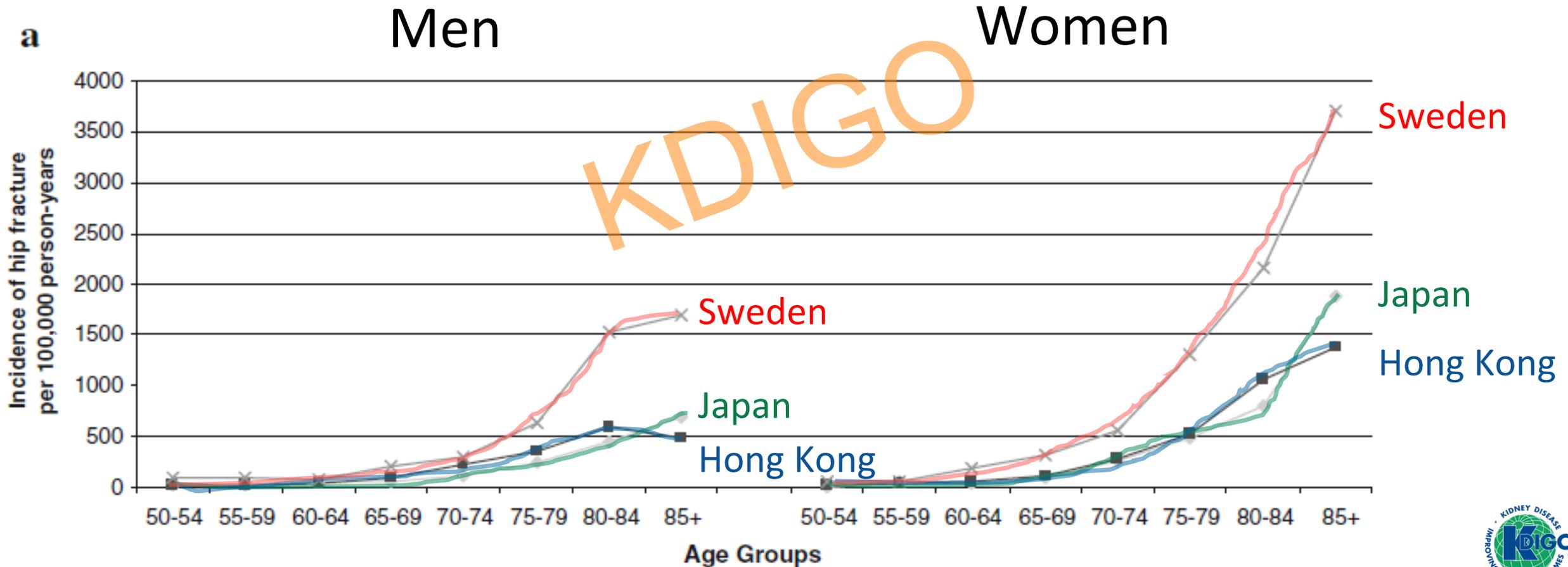


Dialysis patient-specific factors

A beta-2M-amyloidosis and related osteopathy, CKD-MBD, dialysis modality, etc.

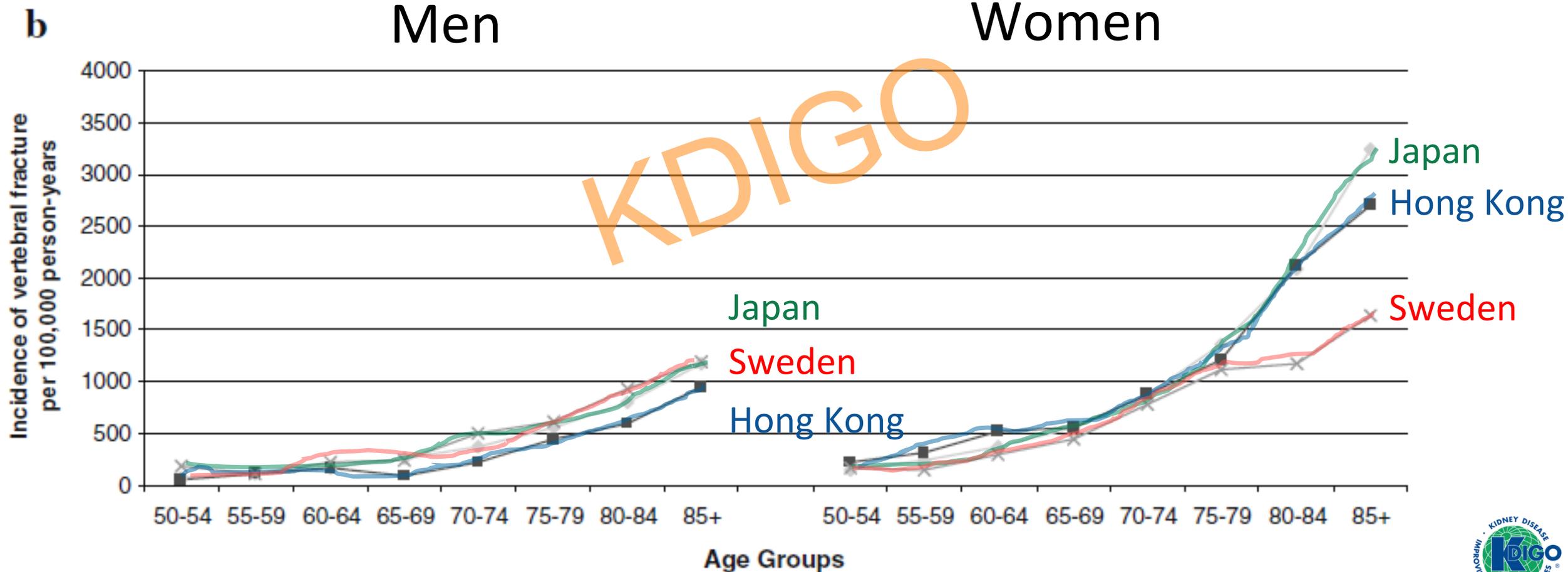
AGE-SPECIFIC INCIDENCE RATES IN HONG KONG COMPARED TO JAPANESE AND SWEDISH CAUCASIANS FOR HIP FRACTURE

Bow CH, et al. *Osteoporos Int* 23:879–885, 2012



AGE-SPECIFIC INCIDENCE RATES IN HONG KONG COMPARED TO JAPANESE AND SWEDISH CAUCASIANS FOR CLINICAL VERTEBRAL FRACTURE

Bow CH, et al. *Osteoporos Int* 23:879–885, 2012



OUTLINE

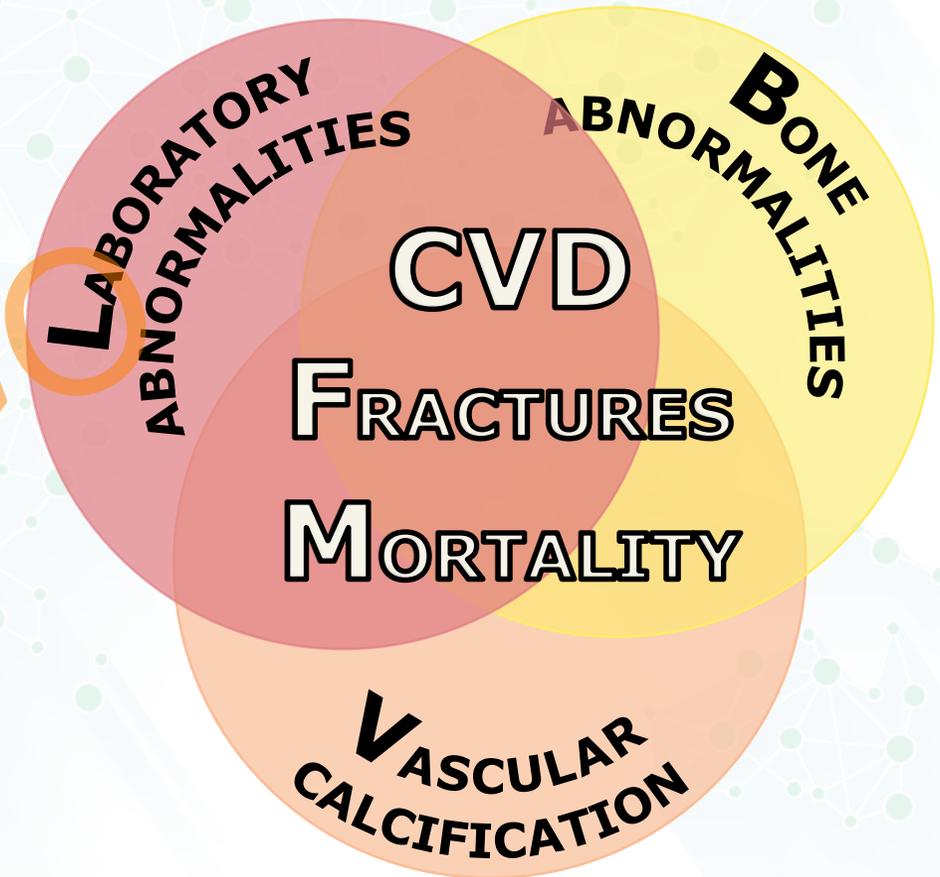
Hip fracture

- Poor survival
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Vertebral fracture



CHRONIC KIDNEY DISEASE MINERAL AND BONE DISORDER



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