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ASSOCIATION OF INCIDENT DIALYSIS MODALITY WITH PATIENT SURVIVAL: A SYSTEMATIC REVIEW AND META-ANALYSIS

06/MEDS-08/B - Nefrologia

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“Je peux perdre une bataille, mais je ne perdrai jamais une minute”

(N.B.)

To my Beloved Family:

to my Caring Mom,

to my Inspiring Dad,

to my Twin Soul,

to my Older Doctor.

To my Infinitely Enthusiastic Mentor.

To the Everlasting Life of my Life ∞

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1. ABSTRACT

Background: Although the choice of dialysis technique is based on several factors, patient survival is undoubtedly one of the most relevant. In a context where randomization to either peritoneal dialysis (PD) or hemodialysis (HD) proved to be extremely challenging, previous meta-analyses were greatly limited due to the inclusion of historical studies.

Methods: We performed a systematic review by searching multiple databases up to April 22nd, 2022. The primary outcome was the association between dialysis modality (PD vs HD) and mortality assessed via hazard ratios (HR). Subgroup analyses were conducted to explore potential sources of heterogeneity, including sex, age, diabetes, dialysis vintage, geographical location, HD access, and study cohort inclusion period.

Results: Database search yielded 5317 citations, from which, 27 observational studies met the eligibility criteria, including 1 033 362 incident dialysis patients. The pooled mortality HR for PD versus HD was 1.01 (95% CI 0.93–1.10). Heterogeneity was substantial (I^2 = 94%) and was largely explained by different baseline features of the included populations. A statistically significant subgroup effect was demonstrated for age (>65 vs.<65 years; p=0.01), geographical location of the studies (Oceania vs. Europe vs. Asia vs. North America; p<0.01), and HD vascular access (central venous catheter vs. arteriovenous fistula; p<0.01, only one study included).

Conclusions: This meta-analysis suggests that overall PD and incentre HD likely carry equivalent survival benefits. However, differences were detected among subgroups based on age, geographic location, HD access type, but not on sex, diabetes status, dialysis vintage and study cohort inclusion period.

2. INTRODUCTION

"The kidney is a truly fascinating organ. It performs miracles quietly and tirelessly, until it doesn't".

2.1 Chronic kidney disease: definition and epidemiology

An aging population and modern lifestyle risk factors accompanied by a decline in early-life infectious diseases have resulted in the rise of chronic diseases as a predominant global health threat with profound socioeconomic and public health consequences[1,2].

Chronic kidney disease (CKD) is a progressive condition characterized by structural and functional changes to the kidney due to various causes. Chronic kidney disease is typically defined as a reduction in kidney function, an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73m², or markers of kidney damage, such as albuminuria, hematuria, or abnormalities detected through laboratory testing or imaging and that are present for at least 3 months[3]. Chronic kidney disease is often underrecognized by patients and clinicians[4–7]. Defined by a glomerular filtration rate (GFR) of less than 60 mL/min/1.73m^2, albuminuria of at least 30 mg per 24 hours, or markers of kidney damage (e.g. hematuria or structural abnormalities such as polycystic or dysplastic kidneys) persisting for more than 3 months,5 CKD is more prevalent in low- and middle-income than in high-income countries[8].

Globally, CKD is most attributed to diabetes and/or hypertension, but other causes such as glomerulonephritis, infection, and environmental exposures (such as air pollution, herbal remedies, and pesticides) are common in Asia, sub-Saharan Africa, and many developing countries. Genetic risk factors may also contribute to CKD risk[9–11].

The global burden of CKD is substantial and growing, with approximately 10% of adults worldwide affected by some form of CKD, resulting in 1.2 million deaths and 28 million years of life lost each year[12,13].

2.2 Kidney replacement therapy

Chronic kidney disease (CKD) is a progressive and irreversible condition that ultimately leads to end-stage renal disease (ESRD). Kidney replacement therapy (KRT), in the form of chronic dialysis or kidney transplantation, is essential for sustaining life in individuals with ESRD. Kidney transplantation is considered the gold-standard treatment of ESRD. However, due to the shortage of donor kidneys and the presence of comorbidities that may preclude transplantation, dialysis remains the predominant treatment option for most patients with ESRD[1,12–14].

2.2.1 Kidney Transplantation

Kidney transplantation remains the treatment of choice for patients with ESRD, as it provides superior survival, better quality of life, and lower long-term healthcare costs compared with dialysis[15–20]. Advances in surgical techniques, immunosuppressive regimens, and donor organ management have markedly improved graft and patient outcomes over recent decades. However, transplantation is not feasible for all patients. Many are excluded due to advanced age, severe comorbidities, or contraindications to immunosuppression, while others remain on prolonged waiting lists due to the persistent shortage of donor organs. As a result, the majority of patients with ESRD worldwide depend on dialysis—either HD or PD—as long-term renal replacement therapy. Dialysis thus plays a dual role: for some patients it is a definitive, lifelong treatment, while for others it serves as a bridge to transplantation. Understanding the comparative effectiveness of HD and PD is therefore essential to optimize patient outcomes, particularly in populations where access to transplantation is limited.

2.2.2 Hemodialysis

Hemodialysis is an extracorporeal technique in which blood is pumped from the patient through a dialyzer containing a semipermeable membrane, where solute and fluid exchange occur with dialysate before the blood is returned to the circulation. Treatments are most performed in-center, typically three times per week, each session lasting 3–5 hours, although home hemodialysis and intensified regimens are increasingly adopted in selected populations. While HD provides efficient clearance of uremic toxins and rapid correction of electrolyte or fluid imbalances, it requires permanent vascular access and is associated with intradialytic hemodynamic instability, vascular access complications, and reduced patient autonomy[21].

2.2.3 Peritoneal dialysis

Peritoneal dialysis, by contrast, is a home-based therapy that uses the patient's peritoneal membrane as the dialysis surface. A catheter implanted in the peritoneal cavity allows infusion of dialysis solution, which dwells for a prescribed time before being drained, carrying with it waste solutes and excess fluid.

The therapy is performed by instilling an osmotically active dialysis fluid into the peritoneal cavity; this solution remains for a prescribed period ("dwell time") until it is drained and replaced with fresh dialysate. Each of these procedures in which the dialysate is drained and infused is known as an "exchange". Normally, this result in excess fluid from plasma circulating in the peritoneal capillaries being drawn across the peritoneal membrane and into the dialysate by osmosis (ultrafiltration). Small (e.g. creatinine, urea nitrogen, potassium and phosphate) and large (e.g. albumin) molecular weight solutes are removed into the dialysate by diffusion and convection. Patients are prescribed suitable number of exchanges, therapy volume and strength solution to achieve adequate level of solute/fluid removal over the course of 24 hours.

PD can be performed manually throughout the day (continuous ambulatory PD, CAPD) or automatically using a cycler, usually overnight (automated PD, APD). The technique is less invasive in terms of vascular access, offers greater flexibility and independence, and better preserves residual renal function compared to HD. However, PD carries specific risks, such as peritonitis, catheter-related infections, and progressive peritoneal membrane dysfunction, which may limit long-term effectiveness.

2.2.4 Hemodialysis vs Peritoneal dialysis: epidemiology and patient survival

Hemodialysis was first successfully performed in the 1940s following the pioneering work of Willem Kolff, who developed the first practical dialysis machine. It became a routine therapy in the 1960s with the introduction of chronic vascular access (the Scribner shunt), which enabled long-term use[22,23].

Peritoneal dialysis was introduced clinically in the 1950s and popularized in the 1970s with the development of long-term indwelling catheters and commercially prepared dialysate[24–34].

Subsequently, in the 1980s, the widespread of PD into clinical practice, initially raised the question of which dialysis modality, between PD and HD, should be preferred[34,35].

According to the United States Renal Data System and the Global Burden of Disease studies, more than 4 million people worldwide are currently receiving chronic dialysis[1,8,12,13]. HD is by far the predominant modality, with ~85–90% of patients on HD and only 10–15% on PD globally[36,37]. However, distribution varies considerably across regions: PD accounts for ~25–30% of patients in countries such as Hong Kong, Mexico, and New Zealand, but less than 10% in North America and most of Europe[38,39]. In the United States, ~88% of dialysis patients are treated with HD, whereas in

Hong Kong and Thailand PD-first policies make PD the primary modality[40–42]. These differences reflect healthcare infrastructure, reimbursement systems, physician practices, and patient preferences.

Although multiple factors influence dialysis modality choice, patient survival remains a top priority for both clinicians and patients. The SONG-PD initiative lists mortality among the five core outcomes that should be reported in all PD studies[43]. A multinational study of patients and caregivers from Australia, the United States, and Hong Kong similarly identified survival as a key treatment goal[44]. Hole' s analysis of dialysis preferences demonstrated that even older patients prioritize treatments that extend survival if independence, treatment location, and frequency are acceptable[45]. Reflecting this consistent emphasis on survival, our meta-analysis focused on all-cause mortality as one of the most universally relevant endpoints for comparing PD and HD in contemporary practice.

Several observational studies have previously compared PD and HD in the ESRD population, but the survival benefit of one modality over the other has not yet been determined since results conflict across studies[46–51].

Moreover, although the results were analyzed after stratification by factors such as age, diabetes status, and dialysis duration, patient subgroups that might derive a greater survival benefit from either PD or HD have not yet been clearly identified.

To date, only two randomized controlled trials attempted to compare mortality risk between the two dialysis modalities. However, the first investigation was halted prematurely due to insufficient enrollment[52], while in the second study the primary outcome was changed to health-related quality of life due to insufficient statistical power[53]. Those results showed the enormous challenge, if not the impossibility, to perform an adequately powered random allocation in this setting.

To overcome this hurdle, few meta-analyses aimed at summarizing the evidence deriving from observational studies have been carried out[54–59]. Nevertheless, all these papers included historical cohorts and were mainly restricted either to elderly populations or individuals with diabetes.

However, in the new millennium the fast spread of automated peritoneal dialysis (APD) in clinical practice, along with the advent of icodextrin[60], promoted a better patient fluid control contributing to solve the problem of fast transport in PD[61–64]. During the same period HD-specific improvements have also occurred with the introduction of biocompatible membranes and the diffusion of on-line high-flux hemodiafiltration[65,66].

However, over the last two decades, a consistent and substantial reduction in mortality rates for patients starting PD has been reported, although such improvements were not observed for HD patients[67]. This differential change in outcomes mandates a new analysis focused on populations treated with modern dialytic techniques to reflect the current therapeutical standards. Hence, whether HD or PD provides a survival advantage to patients with ESRD still remains an unresolved issue.

3. METHODS

3.1 Data source

A comprehensive search of several databases was performed on April 22nd, 2022. Date limits were applied from 2000 forward. Animal studies were excluded. Databases searched were Ovid MEDLINE(R) 1946 to Present and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, Ovid Embase 1988+, Ovid Cochrane Central Register of Controlled Trials 1991+, Ovid Cochrane Database of Systematic Reviews 2005+, Web of Science Core Collection via Clarivate Analytics (1975+), and Scopus via Elsevier (1788+). The search strategy was designed and conducted by an experienced librarian with input from the study's investigators. Controlled vocabulary supplemented with keywords was used to search for studies describing the association of incident dialysis modality with patient survival. The actual strategy listing all search terms used and how they are combined is available below. Citations were managed with the reference management program, Covidence®, while data were first collected in Microsoft® Excel v.16.86 and then analysed through R statistical software [version 4.4.0; meta package; general code: metagen(data, log(HR),lower=log(LL),upper=log(UL), sm = "HR" ,fixed = F, method.tau="REML")][68].

This systematic review's protocol was prospectively registered in PROSPERO (No. CRD42022328308). We adhered to the adapted PRISMA guidelines for systematic reviews (checklist available at the end of the text; see "PRISMA CHECKLIST").

3.2 Search strategy

3.2.1 OVID

Database(s): **Embase** 1988 to 2022 Week 15**, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations** 1996 to April 21, 2022**, EBM Reviews -**

Cochrane Central Register of Controlled Trials March 2022**, EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to April 20, 2022 Search Strategy:

#	**Searches**
1	Hemodiafiltration/ or *hemodialysis/
2	(hemodialysis or haemodialysis or hemofiltrat* or haemofiltrat* or hemodiafiltrat* or haemodiafiltrat* or "acid-free biofiltration" or ((renal or kidney) adj1 dialysis)).ti,ab,hw,kw,kf.
3	1 or 2
4	exp Peritoneal Dialysis/
5	((peritoneal or peritoneum) adj3 dialysis).ti,ab,hw,kw,kf.
6	4 or 5
7	3 and 6
8	exp Survival/ or Survival Rate/ or exp survival analysis/
9	exp Mortality/
10	exp Death/
11	Life Expectancy/
12	(surviv* or death or mortality).ti,ab,hw,kw,kf.
13	mt.fs.
14	or/8-13
15	(modalit* or method or methods or technique* or efficacy or efficacious or effective*or versus or choice or choose or chose or chosen or compar*).ti,ab,hw,kw,kf.
16	7 and 14 and 15
17	(modalit* adj7 (dialysis or "renal replacement")).ti.
18	14 and 17
19	16 or 18
20	(conference abstract or conference review or editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or

	news or newspaper article or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts).mp. or conference abstract.st.
21	19 not 20
22	(("animal stud*" or "animal research" or alpaca or alpacas or algae* or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or bats or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or canis or carp or cats or catfish or cattle or chamaeleo* or chameleon* or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or groundhog or groundhogs or hamster or hamsters or hare or hares or heifer or heifers or horse or horses or iguana or iguanas or insect or insects or jellyfish or kangaroo or kangaroos or kitten or kittens or "laboratory animal*" or lagomorph or lagomorphs or lamb or lambs or lemur or lemurs or lemuridae or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or muskrat or muskrats or nematode or nematodes or newt or newts or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or primates or poultry or quail or rabbit or rabbits or rat or rats or reptile or reptiles or rodent or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or swine or tamarin or tamarins or tilapia or tilapias or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or weasel or weasels or wolf or wolves or worm or worms or wrass* or xenopus or "zebra fish" or zebrafish) not (human or humans or patient or patients)).ti,ab,hw,kw.
23	(rat or rats or mice or mouse or murine or pig or pigs or porcine or swine or dog or dogs).ti.

24	22 or 23
25	21 not 24
26	limit 25 to yr="2000 -Current"
27	remove duplicates from 26

3.2.2 SCOPUS via Elsevier

1	(TITLE-ABS-KEY (hemodialysis OR haemodialysis OR hemofiltrat* OR haemofiltrat* OR hemodiafiltrat* OR haemodiafiltrat* OR "acid-free biofiltration" OR ((renal OR kidney) W/ dialysis)) AND TITLE-ABS-KEY ((peritoneal OR peritoneum) W/3 dialysis)) AND (TITLE-ABS-KEY (surviv* OR death OR mortality))
2	INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
3	1 not 2
4	PUBYEAR AFT 1999
5	3 and 4
6	(TITLE-ABS-KEY ((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR

	kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orang-utan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) AND NOT (human OR humans OR patient OR patients)))
7	5 not 6
8	DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh) OR DOCTYPE(ch)
9	7 not 8

3.2.3 Web of Science Core Collection via Clarivate Analytics

1	(TS=(hemodialysis OR haemodialysis OR hemofiltrat* OR haemofiltrat* OR hemodiafiltrat* OR haemodiafiltrat* OR "acid-free biofiltration" OR ((renal or kidney) NEAR dialysis)) AND TS=((peritoneal OR peritoneum) NEAR/3 dialysis)) AND (TS=(surviv* OR death OR mortality))
2	PMID=(0* or 1* or 2* or 3* or 4* or 5* or 6* or 7* or 8* or 9*)
3	1 not 2
4	3 and Timespan: 2000 to 2022
5	TS=((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines

	OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orangutan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) NOT (human OR humans))
6	4 not 5

3.3 Study selection and data extraction

We included studies which satisfied the following inclusion criteria: (i) comprising adult patients (>18 years old) with end-stage kidney on dialysis treatment; (ii) comparing any chronic PD treatment (continuous ambulatory PD [CAPD]; automated PD [APD] and its variants: continuous cyclic PD [CCPD], nocturnal intermittent PD [NIPD], intermittent PD [IPD] and tidal PD [TPD]) *versus* any type of HD and its variants (hemofiltration, hemodiafiltration, acid-free biofiltration); (iii) providing data on mortality for the patients included with an intention-to-treat analysis; (iv) including patients who started dialysis after 2000 (in case of studies including patients before and after 2000, we include them if there were enough data to extract only the patients from 2000 onwards); (v) classifying the patients according to dialysis modality received 90 days post-initiation of therapy; and (vi) with at least 50 patients per group. We excluded studies (i) which evaluate combined HD and PD strategies; (ii) where hemodialysis comprises intensive dialysis (i.e. greater than 3.5 times per week, or greater than 6 hours per treatment); (iii) where the comparison was between home-HD and PD; (iv) which included the comparison in patients coming back to dialysis after kidney transplant failure; (v) where the results were only presented as as-treated analysis; and (vi) where patients who shifted dialysis method were censored or not included.

Two reviewers (L.N. and D.Z.) screened all titles and abstracts independently. Studies included at this level by either reviewer were included for full-text screening by the same reviewer pair. Discrepancies were solved through discussion or by consultation of a third reviewer (M.P.). Extracted data included study design, year of publication, start and end date of patients' inclusion, number of patients for each group (HD and PD), and main characteristics of the included patients (sex, age, presence of diabetes, coronary artery disease [CAD], congestive heart failure [CHF], and peripheral vascular disease).

3.4 Quality assessment and certainty of evidence

Risk of bias assessment was performed using the Newcastle-Ottawa tool for observational studies[69]. Potential disagreements were resolved through discussion. Certainty of evidence (CoE) of the primary outcome was assessed using the GRADE approach[70].

3.5 Statistical analysis

The primary outcome was mortality as assessed by time-to-event analysis and reported using hazard ratios (HR). Therefore, we collected from each study a pre-computed HR and the corresponding confidence interval (CI) comparing PD and HD. HR's and their standard errors were pooled using a generic inverse variance approach and a random-effects model with a restricted maximum likelihood ratio estimator of between study heterogeneity. We planned several a priori determined subgroup analyses to explore heterogeneity. These analyses were based on risk of bias, sex, age, diabetes status, dialysis vintage (duration), geographic location (continent of study origin), dialysis access type, and year of the patients' inclusion in the study. We tested the interaction between subgroups and generated a P value for the difference based on heterogeneity statistic Q[71]. All analyses are performed using R statistical software[68]. Meta-analyses were performed using the R package "meta" and its subgroup analysis function using the "subgroup" argument[72].

4. RESULTS

4.1 Search results and characteristics of included studies

The results of the literature search are presented in the PRISMA flow diagram in Figure 1.

The initial search identified 5317 citations. After duplicate removal and exclusion on title and abstract screening, 249 studies qualified for a full text review. Two hundreds and twenty-two studies were excluded for specific reasons (Fig. 1). Consequently, a total of 27 studies met our eligibility criteria contributing to the final meta-analysis [49–51,73–96]. The characteristics of the included studies are summarized in Table 1.

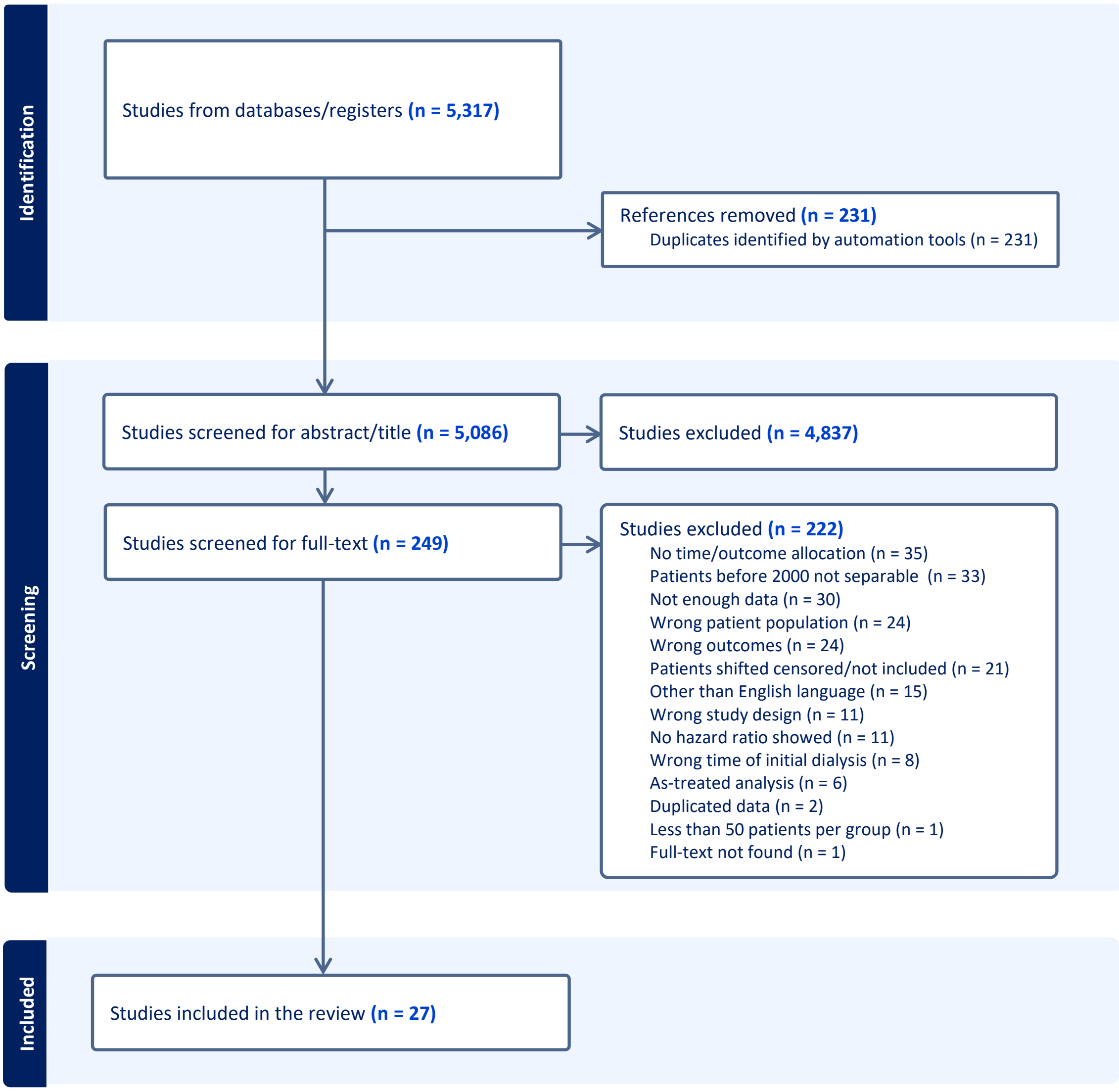


Figure 1 PRISMA flow diagram

AUTHOR	YEAR	COUNTRY	START DATE	END DATE	MATCHED	n total pts	n pts HD	n pts PD
Sunil V.Badve	2014	Australia and New Zealand	2001	2008	no	17022	10860	6162
Chang Jae Hyun	2013	Korea	2000	2009	yes	424	212	212
Couchoud Cecile	2007	France	2002	2005	no	3512	2880	632
Celine Foote	2012	Australia	2002	2005	no	1781	1238	543
Cesar Garcia-Canton	2013	Spain	2005	2010	no	1110	888	222
Mikko Haapio	2013	Finland	2000	2009	no	4463	3246	1217
James Heaf	2014	Denmark	2000	2010	no	7579	5297	2282
Ping-Jen Hu	2021	Taiwan	2006	2015	yes	21492	10746	10746
Jong Cheol Song	2021	Korea	2000	2013	no	21840	15802	6038
Chun Yuan Khoo	2022	Singapore	2007	2012	no	5309	4449	860
Hyunwook Kim	2014	Korea	2005	2008	yes	14098	7049	7049
Murray D. Krahn	2019	Canada	2006	2014	no	12514	9687	2827
Victoria A.Kumar	2014	USA	2001	2013	yes	2006	1003	1003
Mi Jung Lee	2016	Korea	2008	2013	no	902	637	265
Shina Lee	2014	Korea	2005	2008	no	11301	9186	2115
Hanna Lievense	2012	USA	2006	2011	yes	8016	4008	4008
Rajnish Mehrotra	2010	USA	2002	2004	no	252961	233082	19879
Gabriel Mircescu	2013	Eastern Europe	2008	2011	no	9252	8252	1000
Purna Mukhopadhyay	2020	USA	2010	2014	no	130324	82978	47346
Van de Luijtgaarden	2015	Europe	2003	2007	yes	19712	9856	9856
Wagner Martin	2011	United Kingdom	2002	2004	no	3631	2545	1086
Waldum-Grevbo	2015	Norway	2005	2012	yes	1364	682	682
I-Kuan Wang	2016	Taiwan	2000	2010	yes	1950	975	975
Virginia Wang	2021	USA	2006	2013	no	449652	401595	48057
Eric D. Weinhandl	2010	USA	2003	2003	yes	12674	6337	6337
Ben Wong	2018	Canada	2004	2017	no	1376	926	450
Karen Yeates	2012	Canada	2001	2007	no	17097	13244	3853

Table 1 Characteristics of the included studies

HD = hemodialysis; n = number; PD = peritoneal dialysis; pts = patients.

All analyzed papers were retrospective cohort studies published between 2007 and 2021: twenty-two studies were registry-based, three were from multi-center cohorts[77,85,95] and one single-center study[74]. Cohort periods ranged from 2000 to 2015. There was wide geographical variability, with nine studies conducted on North American populations[49,50,83,84,87,89,94–96], an eight on European cohorts[51,75,77,78,88,90–92], an additional eight studies reporting on Asian patients[74,79,81,82,85,86,93,97], and two on dialysis patients from Australia/New Zealand[73,76], as shown in Table 1.

Few studies compared mortality risks in populations with specific characteristics, such as those with either diabetes[85], a previous history of stroke[93] or age > 75 years[75,76].

All included studies enrolled incident patients who initiated dialysis between 2000 and 2017. In total, 1,033,362 patients were analyzed, of whom 847,660 started on HD and 185,702 on PD. Among these, 81,736 patients underwent a matching process in the original studies (Table 1). The main characteristics of the included populations are summarized in Table 2.

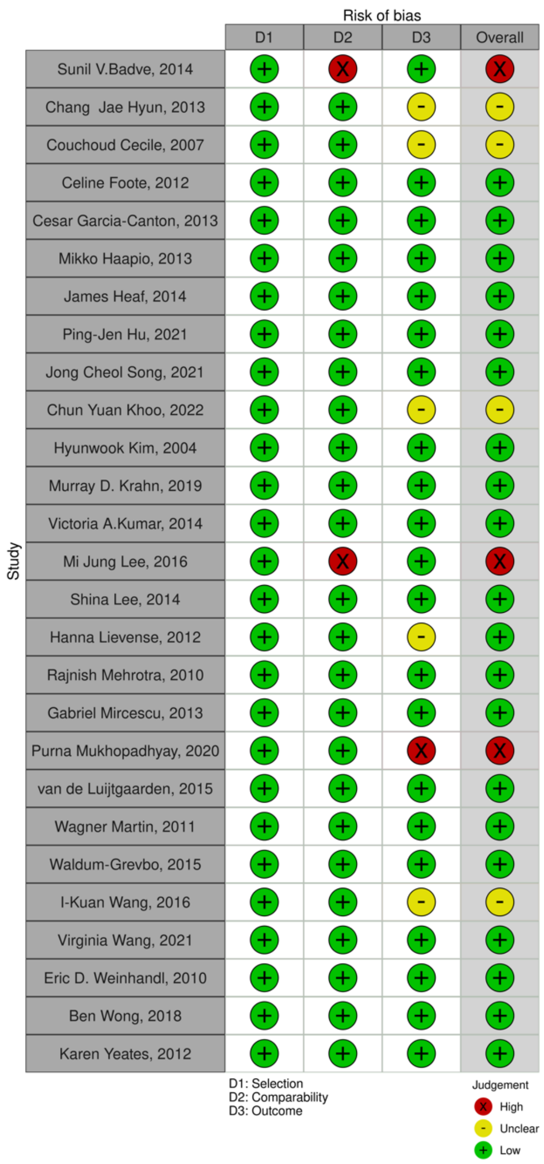
4.2 Risk of bias and study quality

Three studies were considered at high risk of bias primarily due to lack of adjustment for potential confounding variables[73,85,89], while four studies were judged to have unclear risk of bias since the modality of the intention to treat analysis was not explained in detail[74,75,81,93] (Table 3). On the other hand, the remaining 20 studies were deemed at low risk of bias[49–51,76–80,82–84,86–88,91,92,94–96,98].

AUTHOR	COUNTRY	PATIENTS (%)		GENDER male (%)		AGE mean (SD)*		DIABETES (%)		CORONARY DISEASE (%)		CHF (%)		PVD (%)	
		HD	PD	HD	PD	HD	PD	HD	PD	HD	PD	HD	PD	HD	PD
Sunil V.Badve	Australia and New Zealand	10 860 (63.8)	6162 (36.2)	6793 (62.6)	3456 (56.1)	60.6 (15.1)	60.3 (14.7)	4773 (44)	2609 (42.3)	NA	NA	4470 (41.2)	2337 (37.9)	NA	NA
Chang Jae Hyun	Korea	212 (50)	212 (50)	133 (62.7)	132 (62.3)	51.6 (13.8)	52.1 (12.9)	113 (53.3)	121 (57.1)	40 (18.8)	45 (21.2)	33 (15.6)	43 (20.3)	7 (3.3)	5 (2.4)
Couchoud Cecile	France	2880 (82)	632 (18)	HD + PD = 2082 (59.3)		NA	NA	HD + PD = 1264 (36)		HD + PD = 1208 (34.4)		HD + PD = 1324 (37.7)		HD + PD = 1029 (29.3)	
Celine Foote	Australia	1238	543	HD + PD = 1103 (61.9)		HD + PD = 79 (77-81)		HD + PD = 552 (31)		HD + PD = 1063 (59.7)		NA	NA	HD + PD = 579 (32.5)	
Cesar Garcia-Canton	Spain	888 (80)	222 (20)	577 (51.9)	150 (68.5)	59 (20)	66 (19)	521 (58.7)	103 (46.4)	206 (23,1)	46 (20,7)	285 (32)	52 (23.4)	283 (31,9)	56 (25.2)
Mikko Haapio	Finland	3246 (72.7)	1217 (27.3)	2071 (63.8)	783 (64.3)	64.4 (53.9-73.2)	55.2 (43.1-66.7)	1065 (32.8)	532 (43.7)	539 (16.6)	161 (13.2)	386 (11.9)	89 (7.3)	467 (14.4)	100 (8.2)
James Heaf	Denmark	5297 (69.9)	2282 (30.1)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ping-Jen Hu	Taiwan	10746 (50)	10746(50)	5590 (52)	5590 (52)	57.3 (14)	57.3 (14)	4943 (46)	4943 (46)	NA	NA	NA	NA	NA	NA
Jong Cheol Song	Korea	15802 (72)	6038 (28)	9078 (57.6)	3290 (55.5)	54.2 (13.9)	53.7 (13.3)	7235 (45.8)	2706 (44.8)	NA	NA	NA	NA	NA	NA
Chun Yuan Khoo	Singapore	4449 (83.8)	860 (16.2)	2567 (57.7)	403 (46.9)	60 (12.9)	62 (15.3)	3063 (68.9)	615 (71.5)	1908 (42.9)	388 (45.1)	NA	NA	638 (14.3)	125 (14.5)
Hyunwook Kim	Korea	7049 (50)	7049 (50)	4013 (56.8)	4004 (56.9)	54.8 (13.4)	54.6 (13.1)	3685 (52.3)	3602 (51.1)	280 (4.0)	276 (3.9)	1083 (15.4)	1094 (15.5)	371 (5.3)	374 (5.3)
Murray D. Krahn	Canada	9687 (77.4)	2827 (22.6)	5874 (60.6)	1641 (58)	66.8 (14.7)	62.9 (15)	5421 (56)	1468 (51.9)	NA	NA	NA	NA	NA	NA
Victoria A.Kumar	USA	1003 (50)	1003 (50)	543 (54.1)	543 (54.1)	58.4 (13.6)	57.4 (14.2)	486 (48.5)	486 (48.5)	NA	NA	NA	NA	NA	NA
Mi Jung Lee	Korea	637 (70.6)	265 (29.4)	NA	NA	NA	NA	637 (100)	265 (100)	87 (13.7)	43 (16.2)	68 (10.7)	41 (15.5)	55 (8.6)	26 (9.8)
Shina Lee	Korea	9186 (81.3)	2115 (18.7)	NA	NA	NA	NA	HD + PD = 6264 (55.4)		HD + PD = 643 (5.7)		HD + PD = 2158 (19.1)		HD + PD = 938 (8.3)	
Hanna Lievense	USA	4008 (50)	4008 (50)	1863 (46.5)	1807 (45.1)	57.9 (17)	57.6 (16.5)	2203 (55)	2202 (54.9)	781 (19.4)	682 (17)	1137 (23.4)	744 (18.6)	442 (11)	353 (8.8)
Rajnish Mehrotra	USA	233082 (92.1)	19879 (7.9)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Gabriel Mircescu	Eastern Europe	8252 (89.2)	1000 (10.8)	4786 (58)	507 (50.7)	60.7 (60.4-61.1)	60.7 (59.5-61.5)	1246 (15.1)	194 (19.4)	NA	NA	NA	NA	NA	NA
Purna Mukhopadhyay	USA	82978 (69.0)	47346 (31.0)	52573 (63.4)	26912 (56.8)	64.4	56.7	50825 (61.3)	24748 (52.3)	15349 (18.6)	5548 (11.8)	21033 (25.5)	7407 (15.8)	9481 (11.5)	3566 (7.6)
van de Luijtgaarden	Europe	9856 (50)	9856 (50)	6111 (62)	6111 (62)	58.3 (16.9)	58.1 (17)	2503 (25.4)	2405 (24.4)	NA	NA	NA	NA	NA	NA
Wagner Martin	United Kingdom	2545 (70.1)	1086 (29.9)	HD + PD = 2258 (62.2)		HD + PD = 64 (49-73)		HD + PD = 1056 (29.1)		NA	NA	NA	NA	NA	NA
Waldum-Grevbo	Norway	682 (50)	682 (50)	457 (67)	455 (66.7)	65.2 (15)	64.6 (15.2)	209 (30.6)	200 (29.3)	NA	NA	NA	NA	123 (18)	113 (16.6)
I-Kuan Wang	Taiwan	975 (50)	975 (50)	516 (52.9)	523 (53.6)	63.8 (11.9)	63.6 (12.8)	647 (66.4)	648 (66.5)	427 (43.8)	450 (46.2)	326 (33.4)	341 (35.0)	NA	NA
Virginia Wang	USA	401595 (89.3)	48057 (10.7)	231858 (57.7)	27420 (57.1)	61.7 (15.1)	56.3 (15.1)	229015 (57.1)	23792 (49.5)	80790 820.1)	6753 (14.1)	126301 (31.4)	8401 (17.5)	52887 (13.2)	4084 (8.5)
Eric D. Weinhandl	USA	6337 (50)	6337 (50)	3440 (54.3)	3402 (53.7)	59 (15)	59.1 (15)	3099 (48.9)	3086 (48.7)	1299 (20.5)	1312 (20.7)	1324 (20.9)	1312 (20.7)	671 (10.6)	678 (10.7)
Ben Wong	Canada	926 (67.3)	450 (32.7)	571 (61.7)	268 (59.6)	65.3 (16)	64.7 (14.8)	488 (52.7)	207 (46)	326 (35.2)	117 (26)	262 (28.3)	72 (16)	155 (16.7)	48 (10.7)
Karen Yeates	Canada	13244 (87.5)	3853 (22.5)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Table 2 Population characteristics of the included studies

CHF = chronic heart failure; HD = hemodialysis; n = number; NA = not available; PD = peritoneal dialysis; PVD = peripheral vascular disease. *Otherwise, median (interquartile range).



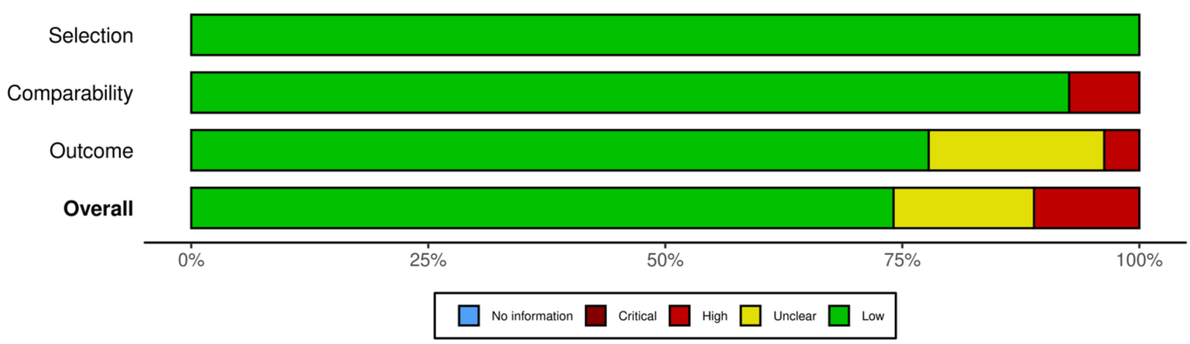


Table 3 Risk of Bias Assessments

From: McGuinness, LA, Higgins, JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411

4.3 Overall mortality

Analysis of all the studies showed no statistically significant difference in mortality between PD and incenter HD (HR=1.06 [95% CI 0.97 – 1.15, I^2 = 94%]), (Fig. 2). There was a significant interaction based on risk of bias, hence, we considered the estimate derived from the 17 studies at low risk of bias to be the best available estimate (HR=1.01 [95% CI, 0.93 – 1.10, I^2 = 94%]. Subsequent subgroup analyses were performed only on studies at low risk of bias.

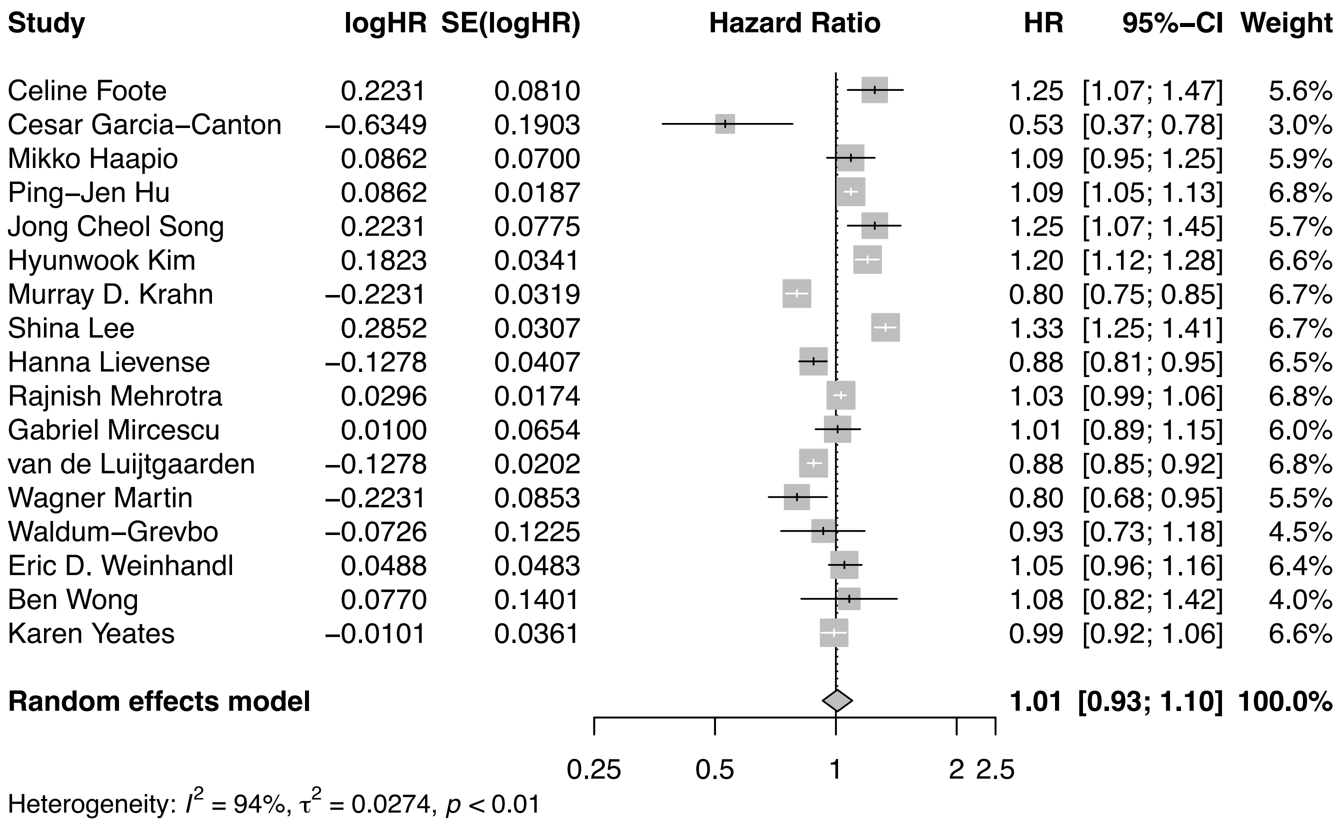


Figure 2 Forest plot for meta-analysis of studies comparing all-cause mortality risk of PD versus in-centre HD.
CI = confidence interval; HR = hazard ratio; SE = standard error.

4.4 Subgroup analyses

When applying an age cut-off of 65 years, we identified a statistically significant subgroup effect (p = 0.01), indicating that age acted as a significant effect modifier and may partially account for the observed heterogeneity. Specifically, in patients younger than 65 years, PD was associated with a significantly lower mortality compared with HD (HR 0.75, 95% CI 0.56–0.99).

There was substantial heterogeneity between the studies within each of these subgroups (age>65: I^2=96%; age<65: I^2=46%).

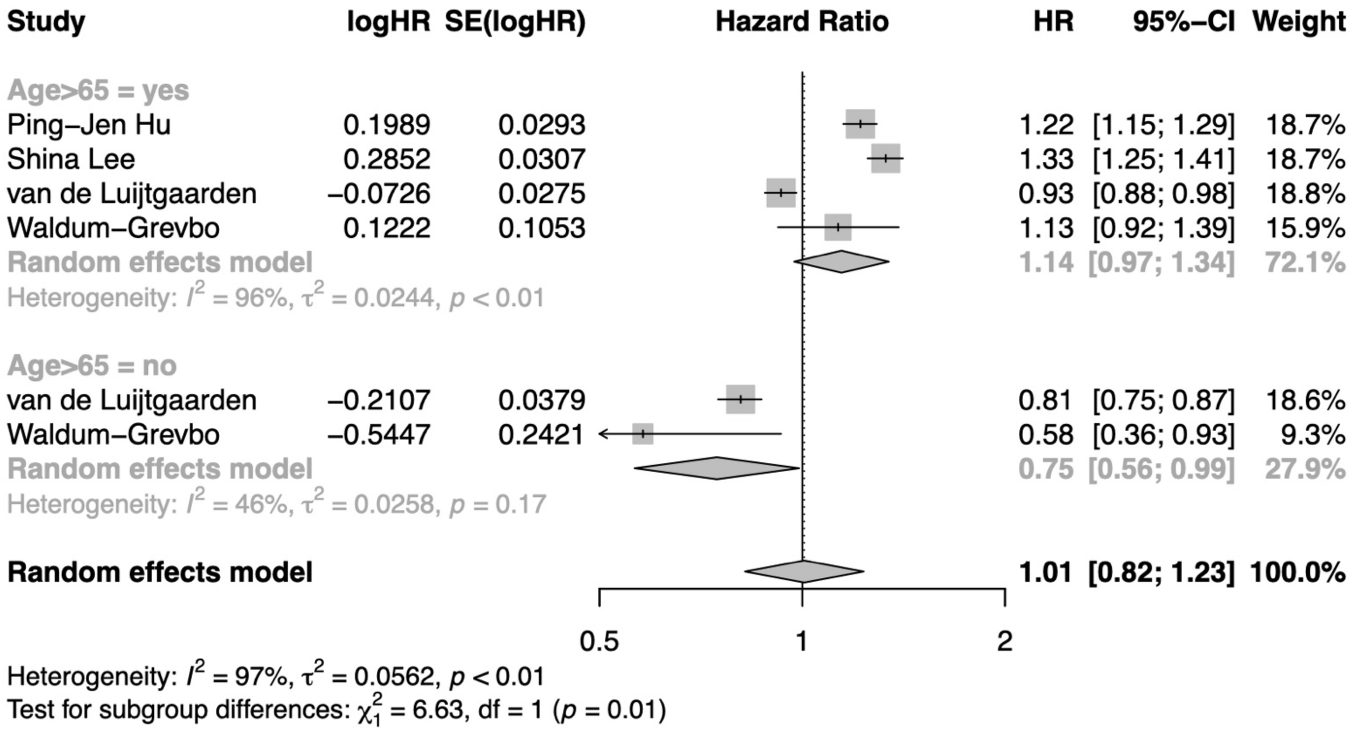


Figure 3 Forest plots for meta-analyses of PD versus HD mortality risk by age.

CI = confidence interval; HR = hazard ratio; SE = standard error.

We also observed a statistically significant subgroup effect when considering the continent of origin of the included studies (Oceania vs. Europe vs. Asia vs. North America; p < 0.01), indicating that geographic location was a significant effect modifier. The lowest HRs were observed in Europe (HR 0.89, 95% CI 0.77–1.03) and North America (HR 0.95, 95% CI 0.87–1.05), suggesting comparable or slightly better survival with PD, whereas higher HRs were reported in Oceania (HR 1.25, 95% CI 1.07–1.47) and Asia (HR 1.21, 95% CI 1.10–1.32), indicating higher mortality with PD in those regions. We detected substantial heterogeneity in each subgroup, except Oceania whose result was based on a single study.

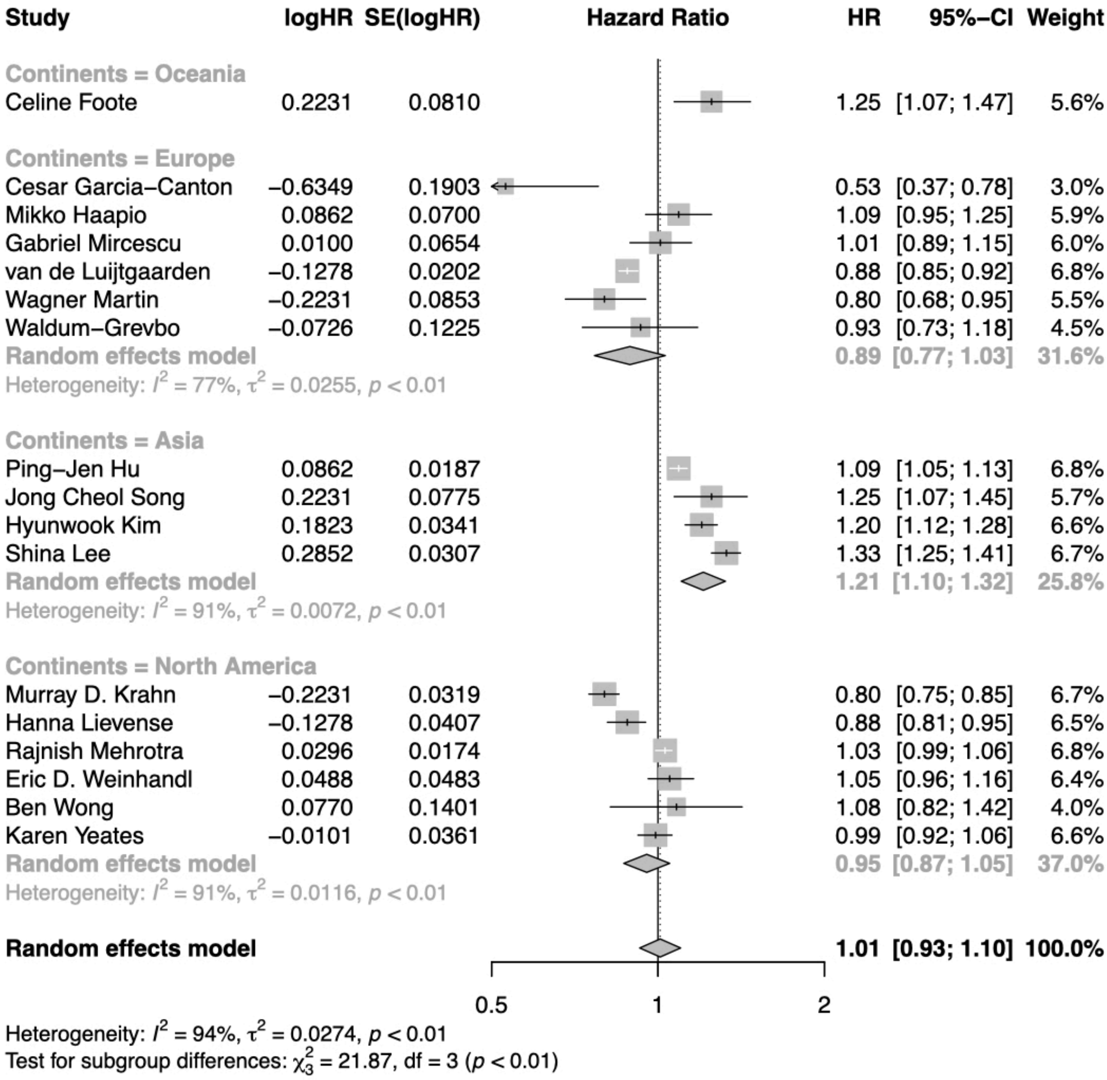
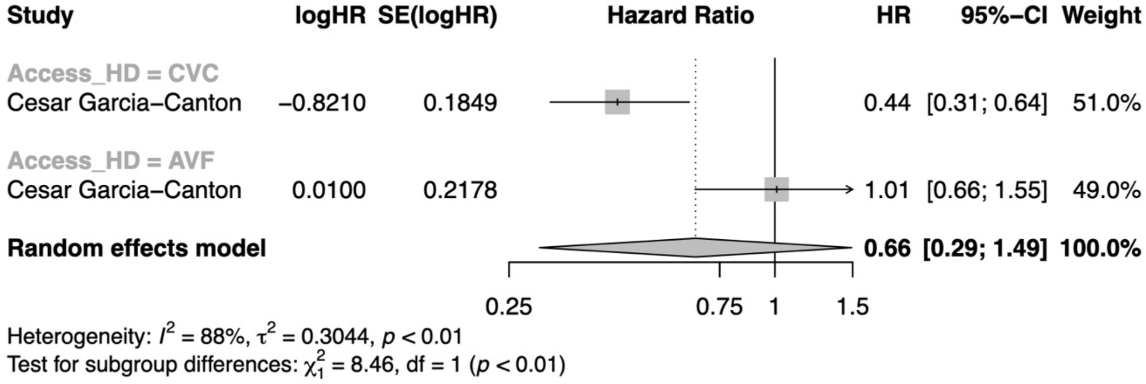


Figure 4 Forest plots for meta-analyses of PD versus HD mortality risk by geographical continent.

CI = confidence interval; HR = hazard ratio; SE = standard error.

There was a statistically significant subgroup effect for the vascular access types in HD (p<0.01), but



this estimate was derived from only one study.

Figure 5 Forest plots for meta-analyses of PD versus HD mortality risk by vascular access.

CI = confidence interval; HR = hazard ratio; SE = standard error.

No statistically significant subgroup effect was found for sex, diabetes, dialysis vintage, and study cohort inclusion period (Figure 3 and Figure 4).

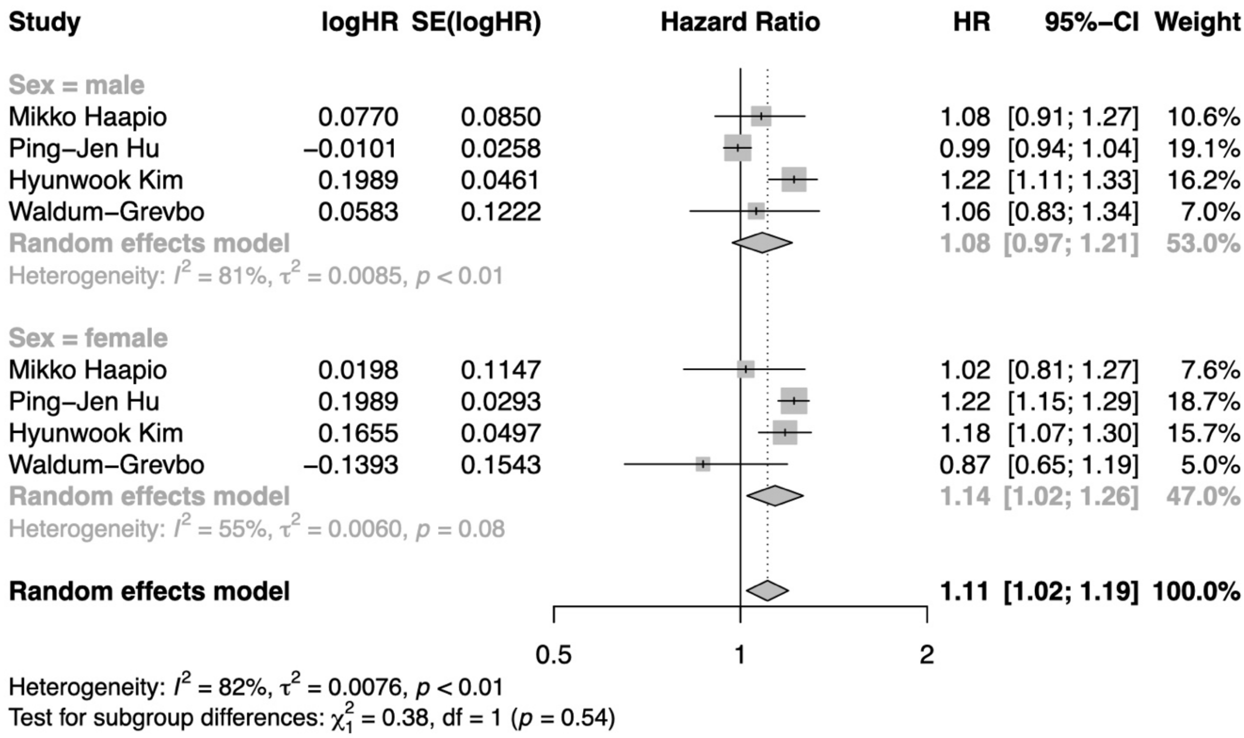


Figure 6 Forest plots for meta-analyses of PD versus HD mortality risk by sex.

CI = confidence interval; HR = hazard ratio; SE = standard error.

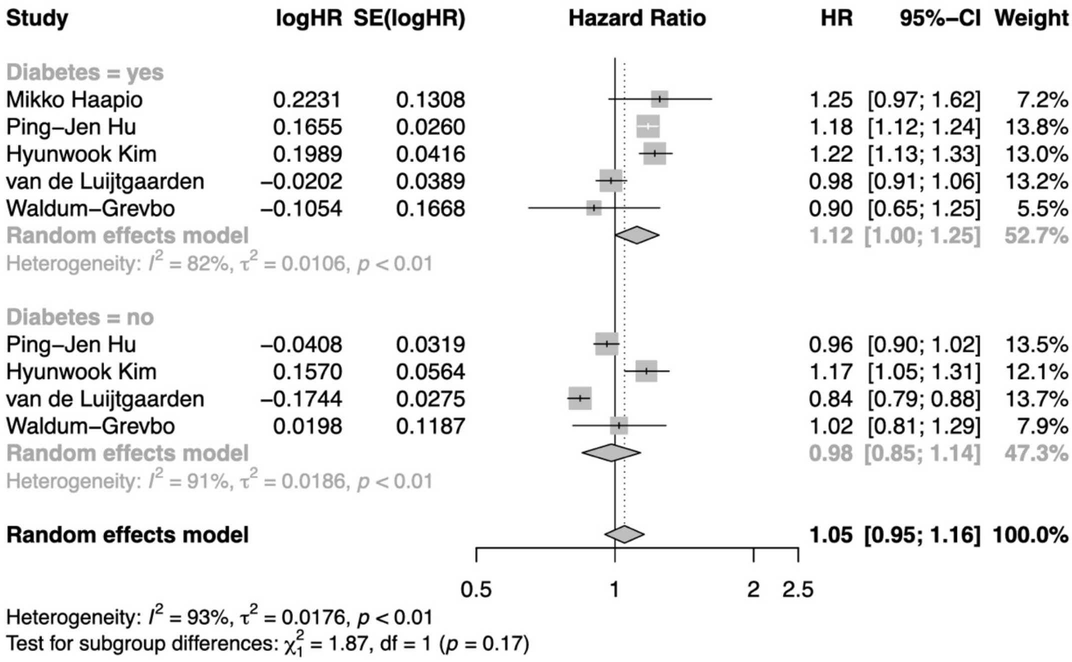


Figure 7 Forest plots for meta-analyses of PD versus HD mortality risk by diabetes status.

CI = confidence interval; HR = hazard ratio; SE = standard error.

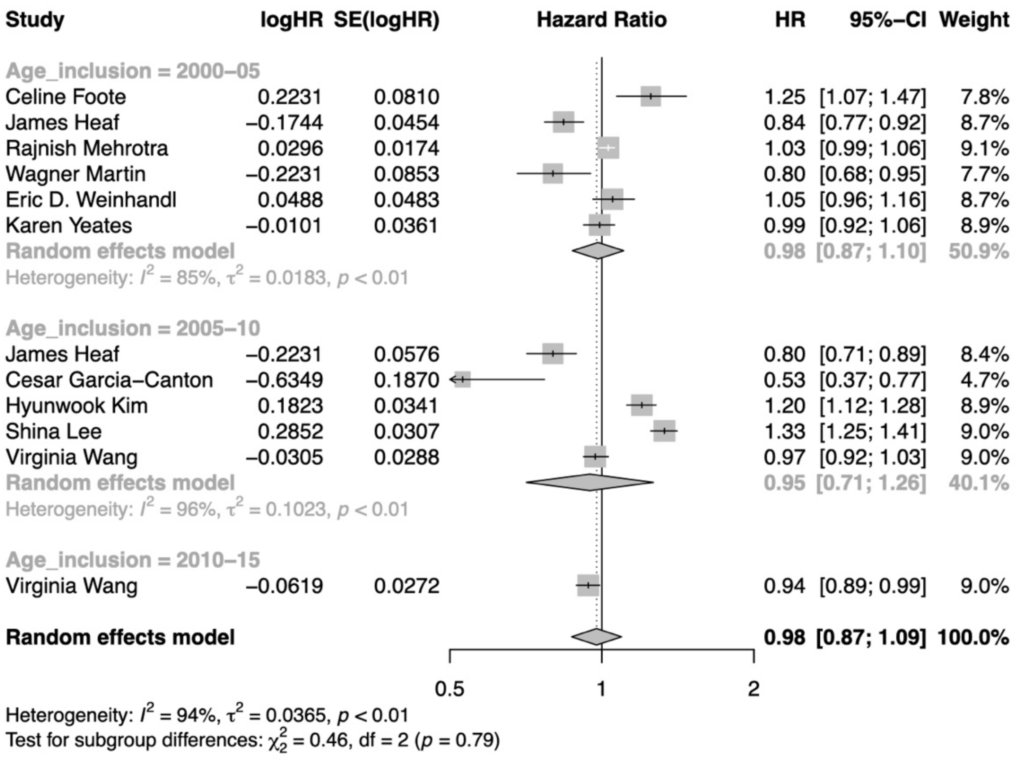


Figure 8 Forest plots for meta-analyses of PD versus HD mortality risk by time period.

CI = confidence interval; HR = hazard ratio; SE = standard error.

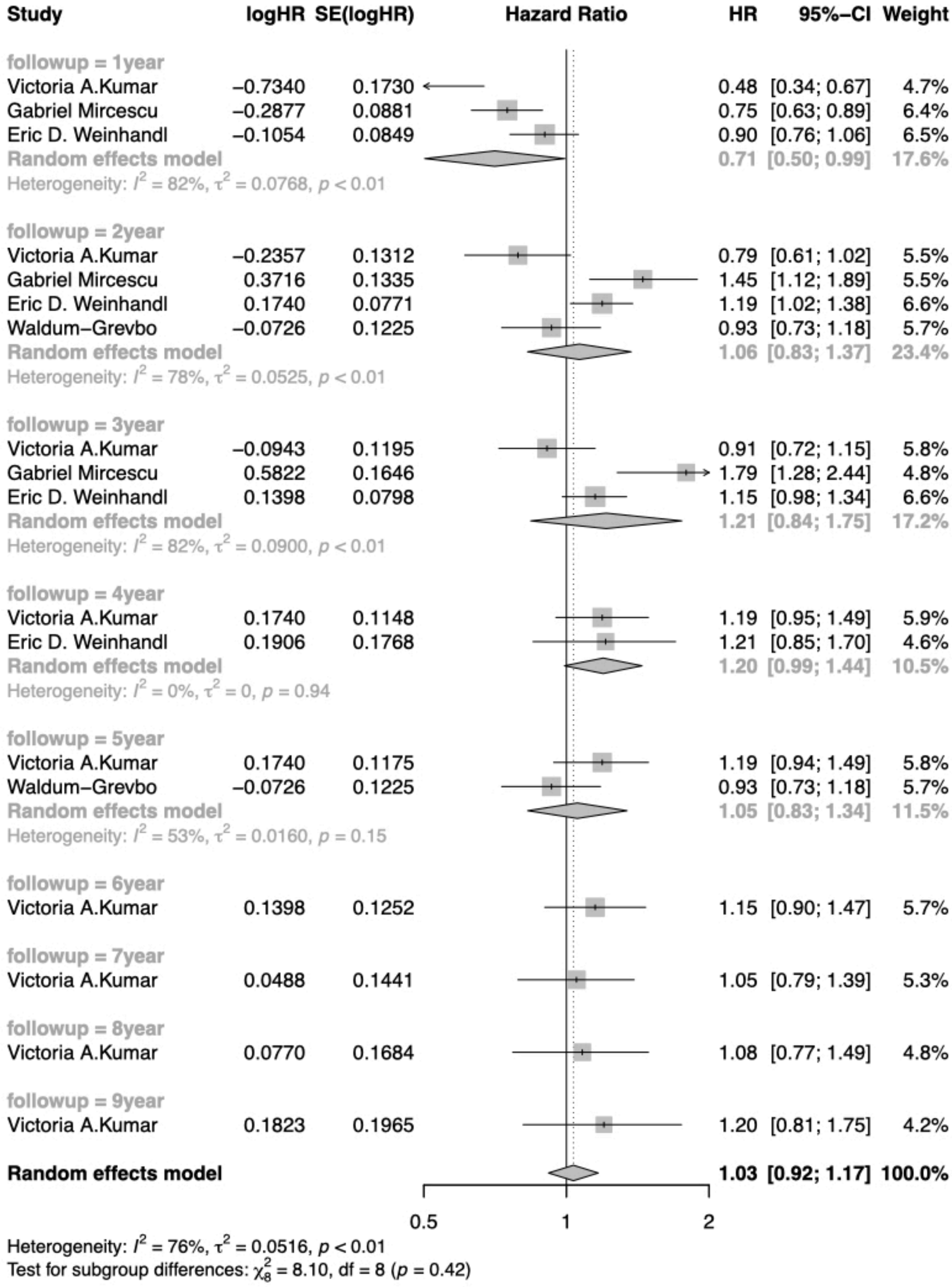


Figure 9 Forest plots for meta-analyses of PD versus HD mortality risk by dialysis vintage.

CI = confidence interval; HR = hazard ratio; SE = standard error.

4.5 Certainty of Evidence

The GRADE evidence profile is shown in table 4. Although the presence of heterogeneity among the studies was adequately explained by different baseline features of the included populations, the final certainty of evidence concerning the primary outcome was graded as low, due to the nonrandomized nature of the available studies.

Question: Peritoneal dialysis (PD) compared to in-centre hemodialysis (HD) for dialysis patients
Setting: Healthcare facilities; different geographical locations

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Peritoneal dialysis (PD)	in-centre hemodialysis (HD)	Relative (95% CI)	Absolute (95% CI)		
17	non-randomised studies	not serious	not serious[a]	not serious	not serious	none	PD=77 908 patients HD=336 774 patients PD/HD HR 1.01 (0.93-1.10)				⨁⨁◯◯ Low[a]	CRITICAL

CI: confidence interval; **HR:** hazard ratio

Explanations
a. Inconsistency explained by the inclusion of studies and patients with different baseline features, such as age, geographical location, and HD access type

Table 4 GRADE evidence profile of the primary outcome (overall mortality PD vs HD patients).

5. DISCUSSION

To the best of our knowledge, this is the first systematic review and meta-analysis to comprehensively investigate the survival benefits of PD compared with in-centre HD based exclusively on contemporary cohorts.

In a context where patients randomization to the two different dialysis modalities proved to be extremely challenging (if not unrealistic)[52,53], previous comparative analysis and systematic reviews of PD/HD mortality were unequivocally limited due to the inclusion of both historical and heterogeneous studies [54–59].

To minimize the effect of selection bias and, at the same time, obtain results which could be reasonably applied to the modern dialytic cohorts, we employed strict inclusion criteria during the process of study selection.

Firstly, we decided to exclude all the data concerning patients who started dialysis before 2000. This year was used as "watershed" since it may correspond to the widespread diffusion of APD[99] and the use of icodextrin in PD practice[100,101] along with the advent of biocompatible membranes and the dissemination of on-line high flux hemodiafiltration [65,66]. In addition, to exclude patients at risk for early mortality we considered only studies that classified patients according to the dialysis modality received 90 days post-initiation of therapy[102,103]. Furthermore, we selected exclusively "intention-to treat" analysis excluding "as-treated" evaluation. "Intention-to treat" analysis allocates patient death based on the starting treatment modality, while "as-treated" analysis allocates patient death according to the treatment modality at the moment of the event. Considering that the rate of transfer of PD patients to HD is significantly higher than the opposite (HD to PD) and that most modality changes are associated with increased mortality after transfers[104,105], we believed that only analysis adjusting for these changes allows to evaluate the effect of initial treatment modality.

A further important consideration in interpreting our findings is the potential for immortal time bias, particularly because modern PD practice often involves earlier initiation with greater residual kidney function, which may independently confer a survival advantage. Unfortunately, comprehensive global data on the prevalence of incremental peritoneal dialysis (IPD) are limited. In Australia and New Zealand, registry data show that IPD use among incident PD patients increased from 2.7% in 2007 to 11.1% in 2017[106]. Similarly, in Italy, Neri et al. reported that the proportion of incident PD patients initiating with IPD rose from 11.5% in 2005 to 27.5% in 2014, reflecting a shift toward earlier and more gradual dialysis initiation[107]. However, data from other regions, including North America, Asia, and Africa, remain scarce, making it difficult to assess global IPD prevalence. This variability is likely influenced by factors such as healthcare infrastructure, clinical practice, and patient demographics. Classifying patients according to dialysis modality at 90 days post-initiation may have mitigated this bias, although it cannot fully eliminate it. Recognized confounders were further addressed through our risk-of-bias assessment, which excluded studies that did not adjust for key variables, and in studies with multivariable analyses, residual renal function had been included in the original studies whenever available.

Despite all these precautions, the level of certainty of the meta-analysis results according to the GRADE profile[70] was unavoidably categorized as “low”, due to the impossibility to include randomized clinical trials.

In our systematic review and meta-analysis we did not find a significant difference in overall mortality risk between PD and in-center HD patients.

However, the HR of death for PD versus in-center HD was heterogenous among cohort studies [I^2 = 94%, P <0.01]. Hence, subgroup analyses were conducted to explore potential sources of heterogeneity, including sex, age, diabetes, dialysis vintage, geographical distribution, HD access, and study cohort inclusion period. The analyses revealed a statistically significant subgroup effect for age, geographical distribution of the individual studies, and HD vascular access.

We observed a significant survival benefit for PD in subjects with an age lower than 65 years. These data strengthened the previous evidence that in young patients PD has a survival advantage over HD[58]. Since PD is a self-management treatment and intraluminal peritonitis is the most frequent and impactful event[108,109], a younger age might help maximize therapy compliance, while minimizing incidence and severity of complications through either a scrupulous execution of the exchanges or/and an early referral of potential hurdles.

Conversely, our results diverge from the common belief that individuals with diabetes present a less favorable survival in PD[57,58]. This condition has been traditionally referred to the constant exposure to glucose in the dialysate that may worsen glycemic homeostasis[110]. Furthermore, individuals with diabetes possess more often a higher peritoneal transport rate that could make more challenging the achievement of volume and adequacy targets[111]. However, the advent of new glucose-sparing dialysates[112], such as icodextrins[113] or amino acids[114], along with the routinary use of APD in clinical practice, may justify these different results. Currently, the renewed interest for free- or low-glucose peritoneal solutions is demonstrated by ongoing clinical trials which aim at evaluating the efficacy and safety of novel xylitol-carnitine and polydextrine-composed peritoneal solutions[115,116]. These novelties along with the technological advancements of systems for PD will require soon a re-evaluation of the outcomes regarding individuals with diabetes on PD.

In addition, our analyses challenge the theory that PD offers a survival advantage during the first year of therapy compared to HD, with this benefit diminishing as dialysis vintage increases [49,84,88,93]. Based on this hypothesis, a "PD-first policy" followed by a planned transition to HD has been proposed[117]. Conversely, the notion of PD as the most suitable bridge to kidney transplantation for potential candidates has been reinforced[118].

Our new data challenge the applicability of these concepts to modern cohorts and discourage transitioning from PD to HD in patients after the first few years of dialytic treatment.

Furthermore, in line with evidence from the last two decades that survival among PD has been superior compared to HD[49,51,67,90,96,119,120], we did not detect a statistically significant subgroup effect for study cohort inclusion period.

As mentioned above, with the emergence of new dialysates and dialyzers, improvement of the ultrafiltration capacity, increased attention to preserving residual renal function and peritoneal membrane integrity, improved dialysis adequacy as well as management of anemia, mineral and nutrition parameters, great advances in PD have been accomplished. These advancements, along with the early evidence, call for future analyses in the coming years focused exclusively on data from the last decade.

It is noteworthy to remark that all the PD advancements previously described are not yet equally accessible worldwide. This observation in combination with additional dissimilarities either in quality of the dialysis modality provided or in patient population characteristics (e.g. prevalence of diabetes in dialysis incident patients) across continents may explain the geographical differences that were observed in our analysis. In fact, we detected a statistically significant subgroup effect when considering the continent of origin of the included studies (Oceania vs. Europe vs. Asia vs. North America). Lowest hazard ratios for mortality comparing PD to HD were observed in Europe (HR 0.89, 95% CI 0.77–1.03) and North America (HR 0.95, 95% CI 0.87–1.05), suggesting similar or slightly better survival with PD in these regions. By contrast, higher HRs were obtained in Oceania (HR 1.25, 95% CI 1.07–1.47) and Asia (HR 1.21, 95% CI 1.10–1.32), indicating that in these regions patients on PD had a significantly higher risk of mortality compared with those on HD—thus reflecting a survival advantage for HD.

Unfortunately, it was not possible to extensively investigate by meta-analysis the effect of HD vascular access types on the relationship of dialysis modality and mortality. The only available study confirms that PD has a clear survival benefit over HD patients starting dialysis with a CVC[77], reinforcing the potentially advantage that PD could confer to subjects who are judged ineligible for arteriovenous fistula creation[103]. Conversely, new data are required to explore the mortality outcome among incident PD patients and subjects initiating HD with an AVF.

Although this systematic review and meta-analysis was conducted according to a rigorous methodology, our study has several limitations. First, it is important to emphasize that the evidence derived from observational studies is inevitably inferior to that from randomized trials. Second, even though most studies attempted to minimize the adverse effects through adjustment, unknown or unmeasured confounders may still undermine the robustness of the outcomes. Third, the potential for immortal time bias and the limited global data on incremental PD represent important constraints, although our methodological approach helped to mitigate these issues. Fourth, as part of the included articles were registry-based, a degree of inherent inaccuracies in coding and record completeness may be expected and population overlapping may exist. Finally, the analysis lacks data from South America, the Middle East, and Africa due to the current unavailability of regional dialysis registries.

These points should be weighed against the meticulous systematic approach of this study, the exclusion of historical cohorts, and the use of numerous and clearly defined inclusion criteria.

In conclusion, evidence derived from the results of this systematic review and meta-analysis evaluating the effect of incident dialysis modality on mortality indicates that, overall, PD and in-center HD carry similar survival rates. However, differences were detected among subgroups. These discrepancies seem to depend mainly on age and continent of origin, but not on sex, diabetic status, and dialysis vintage.

Given the significant challenges and impracticality of conducting randomized controlled trials in this setting, this study offers valuable reassurance that PD and in-center HD provide equivalent overall survival in contemporary cohorts. As such, dialysis modality selection should be individualized, considering patient preferences, clinical characteristics, lifestyle, and access to care. PD may confer a survival advantage in patients under 65 years of age and remains a viable option for individuals with diabetes—challenging earlier assumptions of inferior outcomes in this population. Additionally, PD should be strongly considered for patients without arteriovenous fistula access, given the higher mortality associated with initiating HD via central venous catheter. The findings also challenge the traditional "PD-first, then HD" strategy, as no decline in survival over time was observed among patients maintained on PD. When well-tolerated and clinically effective, PD can be safely continued as a long-term treatment. These results support broader utilization of PD in appropriate patients and reinforce the importance of shared decision-making in selecting dialysis modality.

6. PRISMA CHECK LIST

6.1 PRISMA 2020 MAIN CHECKLIST

Topic	No.	Item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	lines 81-87
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	lines 87-89
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	lines 121-136
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	lines 103-113; Supplementary
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	lines 137-139

Topic	No.	Item	Location where item is reported
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	lines 139-143
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	lines 151-155
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	lines 155-158
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	lines 146-148
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	lines 151-153
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)).	lines 121-136
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	n/a
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Table 1; Table 2

Topic	No.	Item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	lines 153-155
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	lines 155-159
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	lines 189-193
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	n/a
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	lines 147-148
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	lines 164-168; Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1; line 168
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 1; Supplementary

Topic	No.	Item	Location where item is reported
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	lines 189-193
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	lines 197-209
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	lines 189-193
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	n/a
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 3
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	lines 222-225
	23b	Discuss any limitations of the evidence included in the review.	lines 293-307
	23c	Discuss any limitations of the review processes used.	n/a
	23d	Discuss implications of the results for practice, policy, and future research.	lines 313-315
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	lines 117-118
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	lines 117-118

Topic	No.	Item	Location where item is reported
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	n/a
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	In the dedicated section
Competing interests	26	Declare any competing interests of review authors.	In the dedicated section
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	In the dedicated section

6.2 PRISMA ABSTRACT CHECKLIST

Topic	No.	Item	Reported?
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	No
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	No
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes

Topic	No.	Item	Reported?
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	No
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	No
Registration	12	Provide the register name and registration number.	No

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