# Ipertensione

Systematic: Samuele Iesari e Quirino Lai (L’Aquila)

# Linee Guida ERBP 2013

*3.5. On which criteria should we select living kidney donors to optimize the risk–benefit ratio of their donation?*

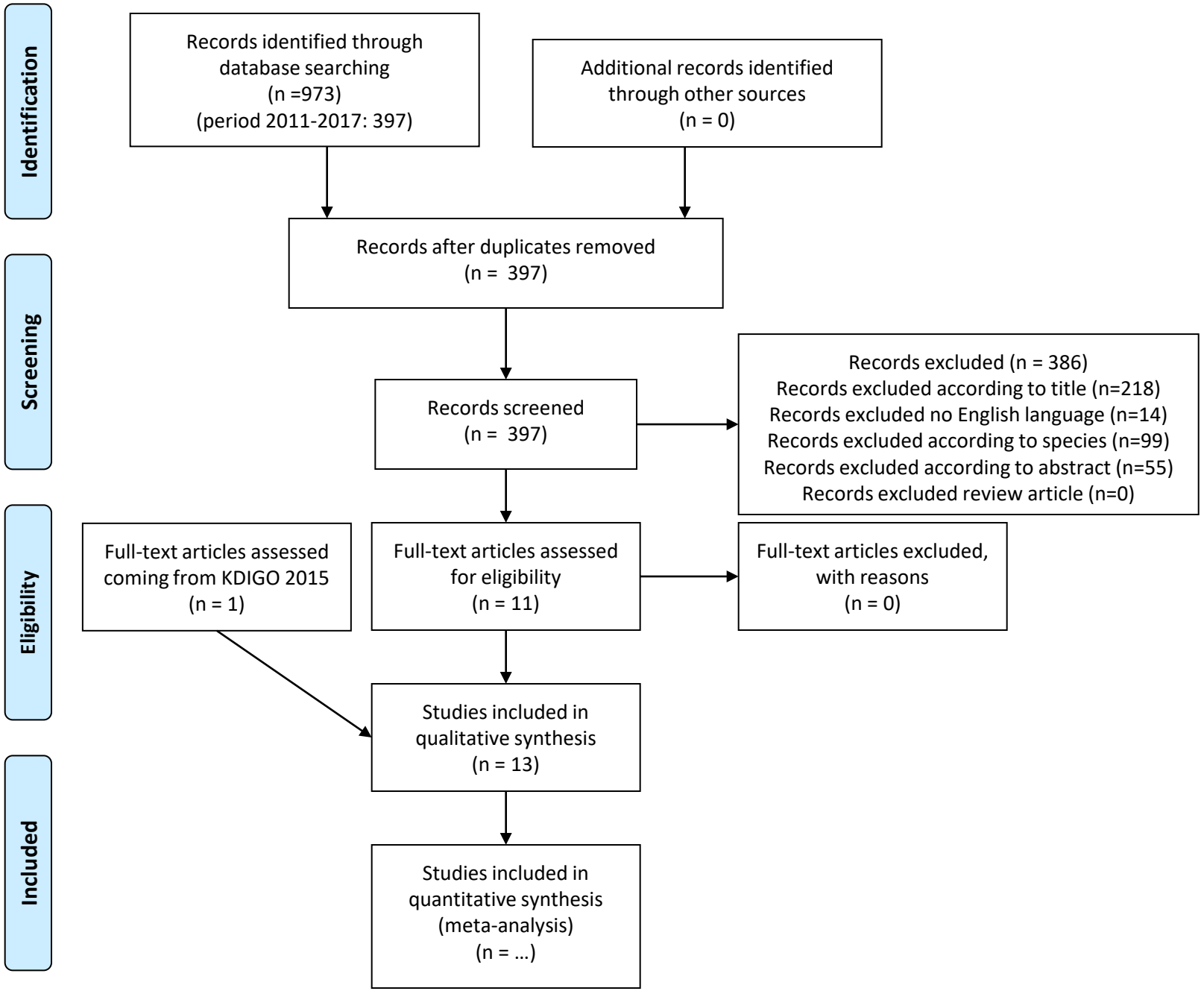
We recommend that the simultaneous presence of more than one risk factor (hypertension, obesity, proteinuria, impaired glucose tolerance, haematuria) precludes donation. (Ungraded Statement)

[…]

**Hypertension**

1. We recommend considering potential donors with a blood pressure <140/90 mmHg on at least three occasions without antihypertensive medication, as normotensive. (1C)
2. We suggest measuring ambulatory blood pressure in potential donors who have office hypertension (blood pressure ≥140/90 mmHg) or who are taking pharmacological treatment for hypertension. (2C)
3. We suggest well-controlled primary hypertension, as assessed by ambulatory blood pressure <130/85 mmHg, under treatment with maximum two anti-hypertensive drugs (diuretics included) is not considered a contraindication to living kidney donation. (2C)
4. We recommend discouraging hypertensive donors with evidence of target organ damage such as left ventricular hypertrophy, hypertensive retinopathy and micro-albuminuria. (1C)
5. We suggest that these potential donors could be re-evaluated for disappearance of this target organ damage after appropriate treatment. (2D)

[…]


Identification
Screening
Eligibility
Included
Records identified through database searching (n =973) (period 2011-2017: 397)
Additional records identified through other sources (n = 0)
Records after duplicates removed (n = 397)
Records screened (n = 397)
Records excluded (n = 386)
Records excluded according to title (n=218)
Records excluded no English language (n=14)
Records excluded according to species (n=99)
Records excluded according to abstract (n=55)
Records excluded review article (n=0)
Full-text articles assessed coming from KDIGO 2015 (n = 1)
Full-text articles assessed for eligibility (n = 11)
Full-text articles excluded, with reasons (n = 0)
Studies included in qualitative synthesis (n = 13)
Studies included in quantitative synthesis (meta-analysis) (n = …)

# Studi selezionati

| Study |
| --- |
| Grams ME, Sang Y, Levey AS, Matsushita K, Ballew S, Chang AR, Chow EK, Kasiske BL, Kovesdy CP, Nadkarni GN, Shalev V, Segev DL, Coresh J, Lentine KL, Garg AX; Chronic Kidney Disease Prognosis Consortium.. Kidney-Failure Risk Projection for the Living Kidney-Donor Candidate. N Engl J Med. 2016 Feb 4;374(5):411-21. |
| Janki S, Klop KW, Dooper IM, Weimar W, Ijzermans JN, Kok NF. More than a decade after live donor nephrectomy: a prospective cohort study. Transpl Int. 2015 Nov;28(11):1268-75. |
| Mjøen G, Hallan S, Hartmann A, Foss A, Midtvedt K, Øyen O, Reisæter A, Pfeffer P, Jenssen T, Leivestad T, Line PD, Øvrehus M, Dale DO, Pihlstrøm H, Holme I, Dekker FW, Holdaas H. Long-term risks for kidney donors. Kidney Int. 2014 Jul;86(1):162-7. |
| Ahmadi AR, Lafranca JA, Claessens LA, Imamdi RM, IJzermans JN, Betjes MG, Dor FJ. Shifting paradigms in eligibility criteria for live kidney donation: a systematic review. Kidney Int. 2015 Jan;87(1):31-45. |
| Tent H, Sanders JS, Rook M, Hofker HS, Ploeg RJ, Navis G, van der Heide JJ. Effects of preexistent hypertension on blood pressure and residual renal function after donor nephrectomy. Transplantation. 2012 Feb 27;93(4):412-7. |

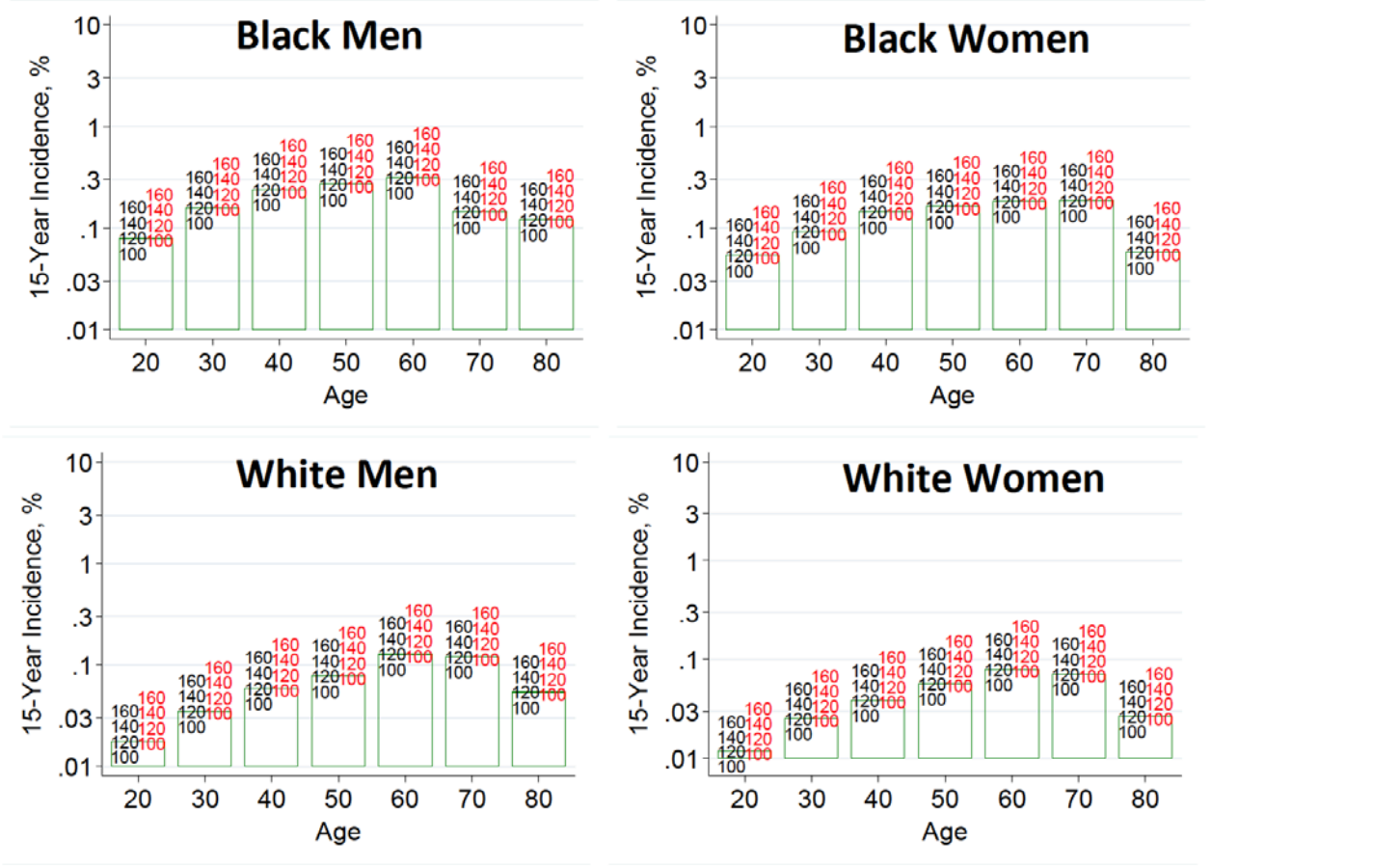
Kidney-Failure Risk Projection for the Living Kidney-Donor Candidate.

Grams ME, Sang Y, Levey AS, et al. N Engl J Med. 2016 Feb 4;374(5):411-21.

- 4,933,314 participants from seven cohorts, followed for a median of 4 to 16 years.
- For a 40-year-old person with health characteristics that are similar to those of age-matched kidney donors, the 15-year projections of the risk of ESRD, in the absence of donation, varies according to race and sex.
- The risk was 0.24% among black men, 0.15% among black women, 0.06% among white men, and 0.04% among white women.
- Risk projections are higher in the presence of:
  - lower estimated glomerular filtration rate,
  - higher albuminuria,
  - hypertension,
  - current or former smoking,
  - diabetes,
  - obesity.
- Higher systolic blood pressure is associated with a higher risk of ESRD: adjusted hazard ratio per increase of 20 mmHg 1.42; 95%CI 1.27-1.58.

[Kidney-Failure Risk Projection for the Living Kidney-Donor Candidate.](#)
Grams ME, Sang Y, Levey AS, et al. N Engl J Med. 2016 Feb 4;374(5):411-21.

**(E) Systolic blood pressure, mmHg without (black) and with (red) antihypertension medication**



More than a decade after live donor nephrectomy: a prospective cohort study.

Janki S, Klop KW, Dooper IM, et al. Transpl Int. 2015 Nov;28(11):1268-75.

- Prospective cohort of 100 donors;
- Median follow-up time of 10 years;
- 9 donors died during follow-up of unrelated causes to donation, and 1 lost to follow-up;
- 9 donors (9%) with pre-existing hypertension, under treatment;
- At follow-up, well regulated blood pressure: median systolic pressure = 133 mmHg, not increased compared to 140 mmHg at baseline (P = 0.307);
- 1 donor still had the same medication, 3 donors received one additional antihypertensive drug, 2 donors received two additional antihypertensive drugs, and 3 switched to other drugs;
- New-onset hypertension present in 23 donors (25.6%), apparently no more frequent compared to the general population;
- At follow-up, median eGFR for donors with pre-existing hypertension = 69.0 ml/min, with new-onset hypertension = 68.7 and without hypertension = 79.9 ml/min (P>0.05): apparently stable renal function.

## Long-term risks for kidney donors.

Mjøen G, Hallan S, Hartmann A, et al. Kidney Int. 2014 Jul;86(1):162-7.

- Comparison of long-term renal function and cardiovascular and all-cause mortality between living kidney donors (median follow up 15.1 years) and a control group of individuals who would have been eligible for donation (median follow up 24.9 years);

- Hazard ratio for all-cause death significantly increased to 1.30 (95%CI 1.11–1.52) for donors compared with controls;
- Significant increase in cardiovascular death to 1.40 (95%CI 1.03–1.91);
- Risk of ESRD greatly and significantly increased to 11.38 (95%CI 4.37–29.6);

- Patients with pre-existing hypertension excluded from analysis! Anyway

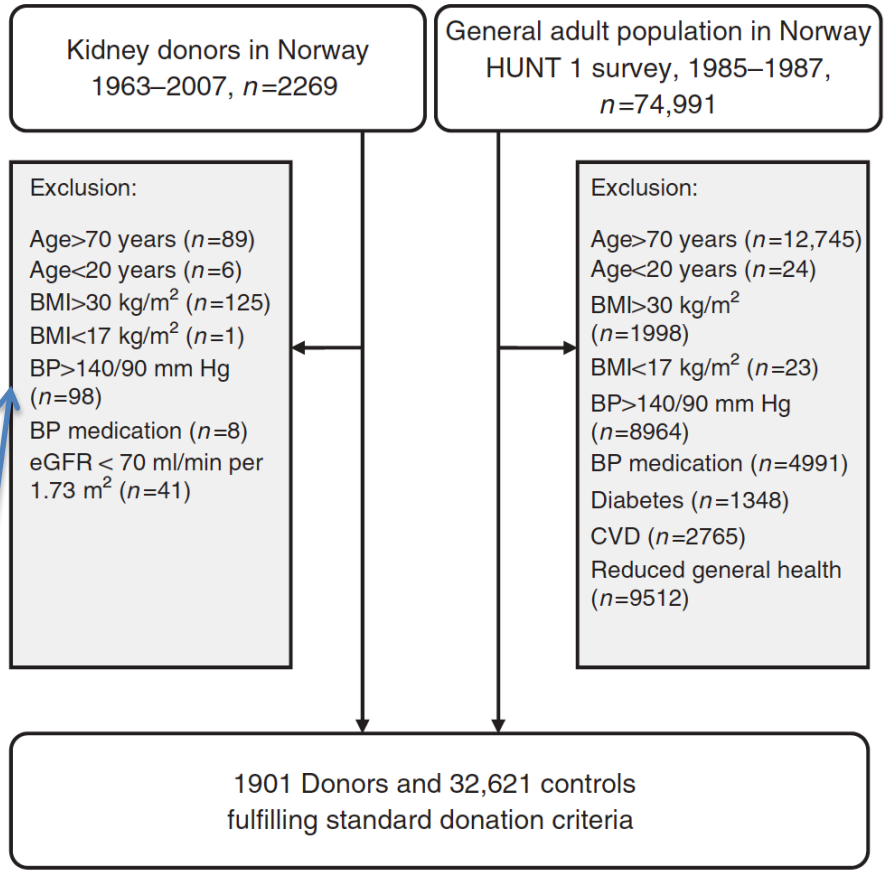



**Figure 1 | Flow chart showing inclusion and exclusion of kidney donors and controls.** BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HUNT 1, Health Study of Nord-Trøndelag.

Long-term risks for kidney donors.

Mjøen G, Hallan S, Hartmann A, et al. Kidney Int. 2014 Jul;86(1):162-7.

**Cox regression analysis for risk of end-stage renal disease in kidney donors versus controls**

| | Unadjusted (n = 25,063–35,222) | | Adjusted 1[a] (n = 31/34,522) | | Adjusted 2[b] (n = 31/34,522) | |
|---|---|---|---|---|---|---|
| Kidney donation | 18.99 | (8.63–41.76, P<0.001) | 11.42 | (4.43–29.40, P<0.001) | 11.38 | (4.37–29.63, P<0.001) |
| Inclusion year | 0.76 | (0.70–0.83, P<0.001) | 0.91 | (0.83–1.00, P=0.04) | 0.90 | (0.82–0.99, P=0.03) |
| Age, years | 1.04 | (1.01–1.07, P=0.003) | 1.03 | (1.00–1.06, P=0.04) | 1.02 | (0.99–1.05, P=0.13) |
| Male | 0.94 | (0.46–1.91, P=0.86) | 1.04 | (0.51–2.11, P=0.10) | 0.90 | (0.43–1.88, P=0.77) |
| Systolic BP | 1.03 | (1.00–1.07, P=0.14) | — | | 1.01 | (1.00–1.06, P=0.03) |
| Smoking | 1.09 | (0.48–2.46, P=0.83) | — | | 1.19 | (0.51–2.76, P=0.68) |
| BMI | 1.19 | (1.02–1.38, P=0.03) | — | | 1.13 | (0.96–1.32, P=0.14) |

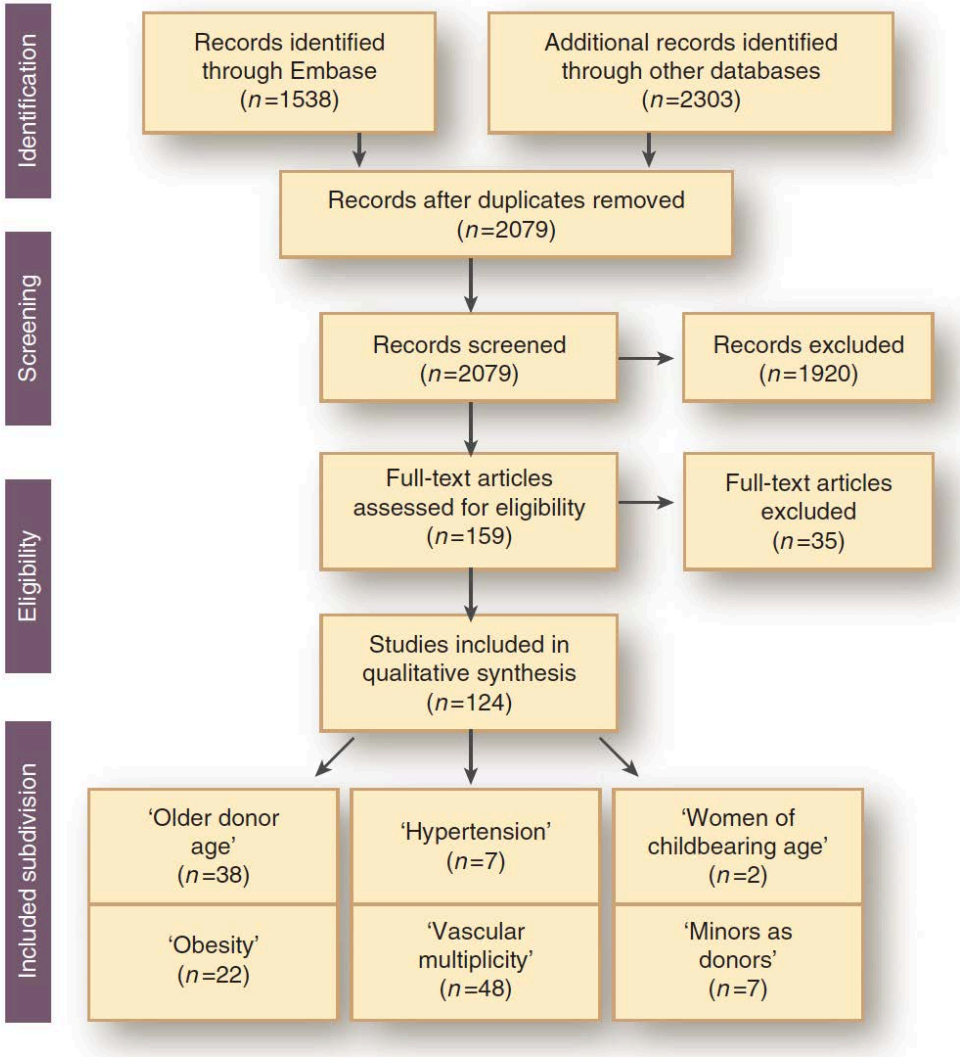
Abbreviations: BMI, body mass index; BP, blood pressure.

[a]Adjusted for age, gender, and year of inclusion.

[b]After multiple imputation and further adjustments for blood pressure, BMI, and smoking.

# Shifting paradigms in eligibility criteria for live kidney donation: a systematic review.

Ahmadi AR, Lafranca JA, Claessens LA, et al. Kidney Int. 2015 Jan;87(1):31-45.




**Live kidney donation of extended criteria live kidney donors**

Patient or population: extended criteria live kidney donors
Settings: several extended criteria as listed below
Intervention: live kidney donation

| Outcomes | No. of participants (studies) | Quality of the evidence (GRADE) | Comments |
|---|---|---|---|
| Women of childbearing age<br>Questionnaires<br>Timing of exposure:<br>0–40 years[1] | 23,325<br>(2 studies[2]) | ⊕⊖⊖⊖<br>Very low[3,4] | 1814 cases and 22,015 controls in case–control studies |
| Hypertension<br>Follow-up: 1–20 years[5] | 81,497<br>(7 studies[6]) | ⊕⊕⊖⊖<br>Low | |
| Obesity<br>Follow-up: 0–5 years[7] | 5924<br>(22 studies[8]) | ⊕⊕⊖⊖<br>Low | |
| Older donor age<br>Follow-up: 0–10 years[9] | 90,027<br>(38 studies[10]) | ⊕⊕⊖⊖<br>Low | |
| Vascular multiplicity<br>Follow-up: 0–10 years[11] | 14,878<br>(48 studies[12]) | ⊕⊕⊖⊖<br>Low | |
| Minors as donors<br>Follow-up: 40 years | 347<br>(7 studies[13]) | ⊕⊖⊖⊖<br>Very low | |

GRADE Working group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[1] Mean time of exposure of the two studies.
[2] Two case-control studies.
[3] Control groups consist of the general population.
[4] Some comparisons were made with the general population.
[5] Median follow-up of 5 years.
[6] Four retrospective cohort studies, two case studies, one review.
[7] Median follow-up of 12 months.
[8] Prospective cohort studies, nine retrospective cohort studies, two case-control studies, two systematic reviews.
[9] Median follow-up of 4.6 years.
[10] Prospective cohort studies, 16 retrospective cohort studies, five case-control studies, four case-series, one review.
[11] Median follow-up of 1.1 year.
[12] Prospective cohort studies, 43 retrospective cohort studies, one discussion.
[13] Retrospective cohort study, one case-series study, one case–control study, two surveys, two reviews.

Shifting paradigms in eligibility criteria for live kidney donation: a systematic review.

Ahmadi AR, Lafranca JA, Claessens LA, et al. Kidney Int. 2015 Jan;87(1):31-45.

- Systematic review combining existing guidelines with available literature until November 2013
- Purpose: establish optimal extended criteria.
- As for hypertension, few articles are available regarding the outcome of accepting hypertensive live kidney donors for donation.
- *Recommendation.*
  - *Hypertension should remain a relative contraindication for live kidney donation.*
  - *Hypertensive live kidney donors with a blood pressure of approximately 140/90mmHg, established by 24-h ambulatory blood pressure measurement and normal renal function, show similar postdonation blood pressure and renal function as normotensive living kidney donors.*
  - *However, based on the evidence available, the exact degree of hypertension and renal function has not yet been established.*
  - *In general, the manageability of the hypertension, the presence of other comorbidities, and overall health determine whether individuals with hypertension should be included or excluded as live kidney donors.*

## Effects of preexistent hypertension on blood pressure and residual renal function after donor nephrectomy.

Tent H, Sanders JS, Rook M, et al. Transplantation. 2012 Feb 27;93(4):412-7.

- Prospective study comparing 47 hypertensive donors and 94 control donors for short-term and 1- and 5-year renal outcomes;
- Matching by gender, age, and body mass index;
- Hypertension defined as predonation antihypertensive drug use;
- Pre- and early postdonation, systolic blood pressure, and mean arterial pressure significantly higher in hypertensive donors;
- Both at 1 year (29 hypertensive donors, 58 controls) and 5 years after donation (13 hypertensive donors and 26 controls) similar blood pressure;
- Renal function similar at all time points;
- Urinary protein excretion similar both pre- and postdonation;
- Mean number of antihypertensive drugs not increased over time;
- At correlation and regression analysis, absence of association between predonation GFR and blood pressure.

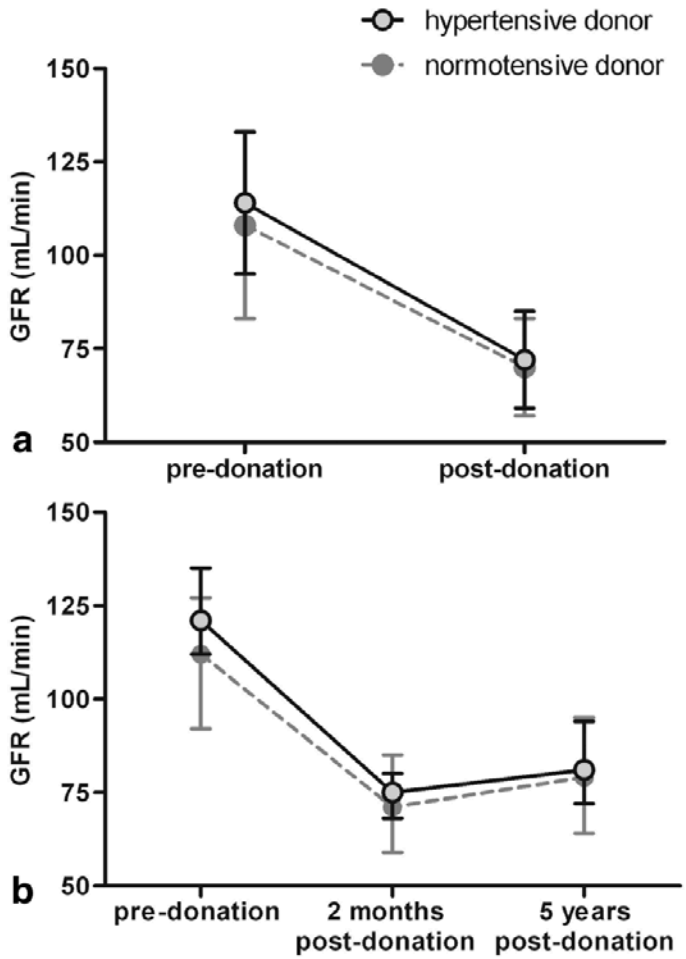



**FIGURE 2.** Change in glomerular filtration rate (GFR) over time. (a) Pre- and 2 months after donation GFR for the whole group (n=141), values represent mean±SD; (b) pre- and 2 months and 5 years after donation GFR for a subset of donors (n=39), values represent median [IQR].