**Supplementary Material**

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| **First Author** | | **Design** | **Primary Outcome** | **EPO used** | Baseline physical HRQOL | | | | | | | | | | | | |  | |  | |  |  |  |  | |  | | |  |  | |  | |  | |  | |  |  |  |  |  |
|  |  |  |  |  | **FACT cont.** | **FACT int.** | **SF-36 vitality cont.** | **SF-36 vitality int.** | **SF-36 Physical Role cont.** | **SF-36 Physical Role int.** | **SF-36 Physical Functioning cont.** | **SF-36 Physical Functioning int.** | **physical KDQOL** | **physical KDQOL** | **Fatigue HRQOL (mean) cont.** | **Fatigue HRQOL (mean) int.** | **Iron use (%)** | | **Ferritin** | | **TST** | **Diabetes (%)** | | **HF (%)** | | **Catheter ( %)** | | **Time on dialysis (yr)** | **Kt/V** | | | **Follow up** | | **Prop IV iron prescript. cont. (%)** | | **Prop IV iron prescript. int. (%)** | | **Main Conclusions** | | | | | |
| **(mean) Cont.** | **(mean) Int.** | **(sd)** | | **(%)** | **(months)** | |
| Churchill, D | | double blind RCT | Six-Minute Walk Test | EPO | - | - | - | - | - | - | - | - | 3.6 | 3.9 | 4.1 | 4.2 | NR | | 1100(1600) | | NR | 0 | | NR | | - | | - | - | | | 6 | | 35 | | 58 | | EPO improves QOL vs. Placebo, but not across EPO targets | | | | | |
| Parfrey, P. S. | | double blind RCT | Left Ventricular Vol. Index | EPO | NR | NR | NR | NR | - | - | - | - | - | NR | NR | NR | NR | | NR | | 36.2 | 18 | | 0 | | - | | - | - | | | 24 | | 25 | | 37 | | Higher Hb target doesn't change LV index or incidence of HF | | | | | |
| Pfeffer, Ma | | double blind RCT | general and CDV mortality | DP | 30.2 | 30.4 | 44.9 (22) | 46.9 ( 23) | 47.5 ( 28) | 47.9 (30) | 44.9 (26) | 45 (27) | - | - | - | - | 42 | | 134 | | 23 | 100 | | 33 | | - | | - | - | | | 38 | | 20.4 | | 14.8 | | Higher Hb target raised cerebrovascular and thrombotic risk | | | | | |
| Roger, Sd | | single blind RCT | Vitality on SF-36 | DP | - | - | 44.5 | 44.4 | - | - | - | - | - | - | - | - | NR | | 235(220) | | 24(8) | 0 | | NR | | - | | - | - | | | 9 | | NR | | NR | | ESA do not improve vitality among elderly CKD patients | | | | | |
| Akizawa, T. | | Open Label | SF-36 and LVMI | EPO-DP | - | - | 65 (20.4) | 63.4 (21.7) | 80.9 (22.8) | 77.2 (26.7) | 76.1 (19) | 73.3 (22.4) | - | - | - | - | NR | | 130 (191) | | 30 (12) | NR | | 7.5 | | - | | - | - | | | 12 | | NR | | NR | | Higher Hb associated with better outcomes on LVMI and HRQOL | | | | | |
| Singh, Ak | | Open Label | Composite outcome CDV | EPO | - | - | 36.6 ( 22.4) | 35.2 (22.6) | 32.5 (29.2) | 31.9 (38.9) | 42.4 (27.3) | 41.9 (28.2) | - | - | - | - | 26.5 | | 173 ( 164) | | 25 (10.5) | NR | | 24 | | - | | - | - | | | 36 | | NR | | NR | | Higher risk for CDV events in higher Hg group. More important in AHF events | | | | | |
| Drueke, T. B | | Open Label | CDV events | EPO | - | - | - | - | - | - | - | - | - | - | - | - | NR | | 181.9 (153) | | 31.8 | 27 | | 33 | | - | | - | - | | | 24 | | NR | | NR | | EPO doesn't reduce CVD events. May improve QOL. | | | | | |
| Rossert, J. | | Open Label | Progression CKD | EPO | - | - | - | - | - | - | - | - | - | - | - | - | NR | | NR | | NR | 34 | | NR | | - | | - | - | | | 7 | | NR | | NR | | EPO may improve QOL. | | | | | |
| Ritz, E. | | Open Label | LVMI | EPO | - | - | - | - | - | - | - | - | - | - | - | - | NR | | 112 | | 22 | 69 | | 3.5 | | - | | - | - | | | 15 | | NR | | NR | | EPO doesn't change LVMI, may improve QOLF | | | | | |
| Villar, E | | Open Label | Progression CKD | EPO-DP | - | - | 39 | 41 | 47 | 46 | 50 | 50 | - | - | - | - | NR | | 167.5 (182) | | NR | 100 | | NR | | - | | - | - | | | 24 | | 0 | | 0 | | EPO doesn't reduce CKD progression. No impact in QOL either. | | | | | |

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| Besarab , Anatole | Open Label | AMI or death | EPO | - | - | 44.7 ( 21.8) | 44.5 ( 22) | 33.3 (38.5) | 33.1 (38.9( | 38.6 (27.5) | 38.6 (26.7) | - | - | - | - | NR | NR | NR | 56 | 100 | 10 | 3.1 | 1.38 | 36 | 75 | 85 | Higher Hb may increase mortality, vascular thrombosis, and QOL |
| Foley, Rn | Open Label | LVVI | EPO | - | - | - | - | - | - | - | - | 3.68 (3.28,4.08) | 3.49 (3.17,3.81) | 4.53 (4.15,4.91) | 4.41 (4.10,4.73) | NR | NR | NR | NR | 100 | 7 | 4.6 | 1.48 | 12 | NR | NR | Higher Hb doesn't improve echocardiographic parameter. May improve QOL |
| Furuland,H | Open Label | HRQOL | EPO | - | - | - | - | - | - | - | - | 4.0(1-7) | 3.83 (1.6-7) | 5 (1-7) | 4.6 (1.17-7) | NR | NR | NR | 20 | 15.5 | - | - | - | 12 | 33 | 59.3 | EPO improves HRQOL. Reaching specified target may reduce mortality |
| Levin | Open Label | LVMI | EPO | - | - | - | - | - | - | - | - | - | - | - | - | 80 | 100 (60-172) | 27(10) | 38 | - | - | - | - | 24 | 11 | 13 | LVMI may not be affected by early anemia treatment |
| McMahon | Double-Blind | NR | EPO | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | Higher Hb may improve LVMI and HRQOL |

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| **First Author** | | **Design** | **Primary Outcome** | **ESA used** | Baseline physical HRQOL | | | | | | | | | | | | |  | |  | |  |  |  |  | |  | |  |  | |  | |  | |  | |  |  |  |  |  |
|  |  |  |  |  | **FACT cont.** | **FACT int.** | **SF-36 vitality cont.** | **SF-36 vitality int.** | **SF-36 Physical Role cont.** | **SF-36 Physical Role int.** | **SF-36 Physical Functioning cont.** | **SF-36 Physical Functioning int.** | **physical KDQOL** | **physical KDQOL** | **Fatigue HRQOL (mean) cont.** | **Fatigue HRQOL (mean) int.** | **Iron use (%)** | | **Ferritin** | | **TST** | **Diabetes (%)** | | **HF (%)** | | **Catheter ( %)** | | **Time on dialysis (yr)** | **Kt/V** | | **Follow up** | | **Prop IV iron prescript. cont. (%)** | | **Prop IV iron prescript. int. (%)** | | **Main Conclusions** | | | | | |
| **(mean) Cont.** | **(mean) Int.** | **(sd)** | | **(%)** | **(months)** | |

Supplementary table 1 : characteristics of included RCTs. EPO : Erythropoeitin. HF : Heart Failure. LV : Left Ventricular. CDV : cardiovascular. LVMI : Left Ventricular Mass Index. QOL : quality of life.

Search Strategy : MEDLINE

(((chronic kidney disease[mesh] OR chronic kidney disease [tiab] OR nephropathy [tiab] OR CKD[tiab] OR chronic renal insufficiency[mesh] OR diabetic nephropathies [mesh] OR

OR Epopen[tiab] OR Globuren[tiab] OR Epoxitin[tiab] OR Nespo[tiab] OR NeoRecormon[tiab] OR Iron therapy[tiab] OR Iron-Deficiency Anemia[mesh] OR Iron\*[tw] OR blood transfusion [mesh] OR hematocrit [tw] OR blood cells [tw])) AND ((Accelerometry [mesh] OR functionality [tiab] OR physical function\*[tiab] OR physical\*[tw] OR fatigue [tiab] OR quality of life [tiab] OR daily living activities [mesh] OR Lawton[tw] OR Katz[tw] OR chronic limitation of activity [mesh] OR independent living [mesh] OR OR disability evaluation [mesh] OR exercise [mesh] OR physical exertion [mesh] OR quality of life [mesh] OR functionality[tw] OR independence [tw] OR dysfunction[tw] OR disability[tw] OR International Classification of Functioning, Disability and Health[mesh] OR SF-36[tw] OR KDQ[tw] OR KDQOL-36[tw] OR accelerometer[tw] OR physical health[tiab] OR physical performance[tw] OR movement[tiab] OR range of motion[tiab] OR daily steps[tiab] OR steps[tiab] OR mobility[tw] OR functional status[tw] OR Sickness Impact Profile Score[tw]))).

Search Strategy : EMBASE

(((‘chronic kidney disease’/exp OR (chronic kidney disease):ab,ti OR (nephropathy):ab,ti OR (CKD):ab,ti OR ‘chronic renal insufficiency’/exp OR ‘diabetic nephropathies’ /exp OR ‘hypertensive nephropathy’/exp OR (diabetic kidney\*):ab,ti OR (kidney dis\*):ab,ti OR ‘chronic renal failure’/exp)) AND (‘anemia’/exp OR (anemia):ab,ti OR (anemia):de,ab,ti OR ‘hemoglobin’/exp OR ‘erythropoietin’/exp OR ‘epoetin alfa’/exp OR (epoetin beta):de,ab,ti OR (epoetin\*):de,ab,ti OR ‘darbepoetin alfa’/exp OR (r-HuEPO):ab,ti OR (EPO):ab,ti OR (erythropoetin recombinant):de,ab,ti OR (human recombinant erythropoietin):de,ab,ti OR (Aranesp:ab,ti) OR (Eprex):ab,ti OR (Epopen):ab,ti OR (Globuren):ab,ti OR (Epoxitin):ab,ti OR (Nespo):ab,ti OR (NeoRecormon):ab,ti OR (Iron therapy):ab,ti OR ‘Iron-Deficiency Anemia’/exp OR (Iron\*):de,ab,ti OR ‘blood transfusion’/exp OR (hematocrit):de,ab,ti OR (blood cells) :de,ab,ti)) AND ((‘Accelerometry’ /exp OR (functionality) :ab,ti OR (physical function\*):ab,ti OR (physical\*):de,ab,ti OR (fatigue) :ab,ti OR (quality of life):ab,ti OR ‘daily living activities’ exp OR (Lawton):de,ab,ti OR (Katz):de,ab,ti OR ‘chronic limitation of activity’/exp OR ‘independent living’/exp OR ‘disability evaluation’/exp OR ‘exercise’ /exp OR ‘physical exertion’/exp OR ‘quality of life’/exp OR (functionality):de,ab,ti OR (independence):de,ab,ti OR (dysfunction):de,ab,ti OR (disability):de,ab,ti OR ‘International Classification of Functioning, Disability and Health’/exp OR (SF-36):de,ab,ti OR (KDQ):de,ab,ti OR (KDQOL-36):de,ab,ti OR (accelerometer):de,ab,ti OR (physical health):ab,ti OR (physical performance):de,ab,ti OR (movement):ab,ti OR (range of motion):ab,ti OR (daily steps):ab,ti OR (steps):ab,ti OR (mobility):de,ab,ti OR (functional status):de,ab,ti OR (Sickness Impact Profile Score):de,ab,ti))).

Quality Score for observational studies : Modified NewCasttle Ottawa scale.

1. Study design

0 Longitudinal retrospective study ( data records)

1 Longitudinal prospective study

1. Representativeness

0 points if included patients from a single center

1 point if included patients from multicenter cohort

1. Ascertainment of Exposure

0 if exposition period not specified

1 if exposition period specified

2) Comparability :

0 points if not adjusted

1 point if adjusted for sex, age and renal function or CKD category

2 points if adjusted for sex, at least one comorbidity , age and renal function

3 points if adjusted for sex, at least one comorbidity, age, renal function and anemia treatment

3) Outcome

0 points if outcome assessments method was not described

1 point if outcome assessments were retrieved from medical records abstraction

2 points if outcome assessments were evaluated by study protocol

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|  |  | Random sequence generation | Allocation concealment | Blinding of participants | Incomplete outcome data | Selective reporting |
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Supplementary Figure 1 : quality of RCTs according to Cochrane tool for risk of bias in RCTs.