

Cancer and chronic kidney disease

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Xue et al: USRDS data '98-'02*

- 31% of subjects with ESRD have a diagnosis of cancer at least two years before start of ESRD treatment
- Control Medicare population has a 21% occurrence rate of cancer

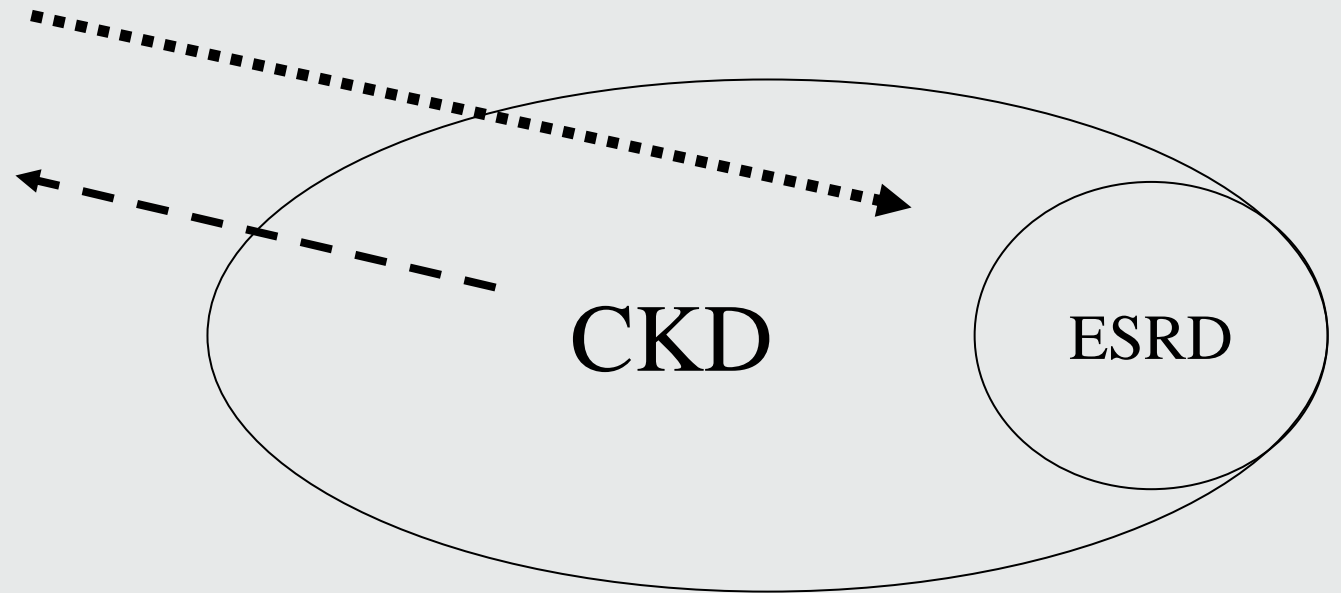
* *Xue JL et al.*

Cancer prevalence in patients with ESRD.

JASN 16:726a, 2005

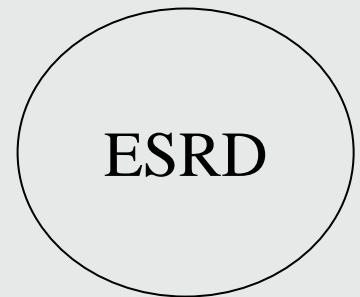
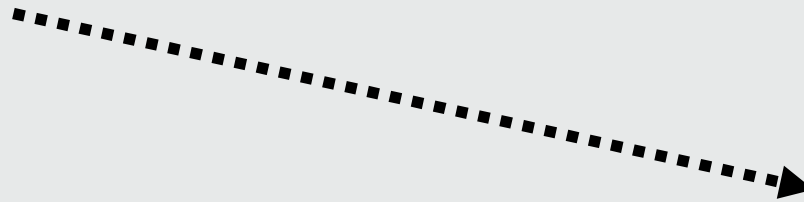
- Cancer could cause ESRD
- CKD could cause cancer

Cancer



Cancer causing ESRD

Cancer



Cancer causing ESRD: the narrow view

- Myeloma
- Nephrectomy for kidney cancer
- Chemotherapy nephrotoxicity
- Bone marrow transplant nephrotoxicity
- Paraneoplastic GN

These sum to only 1.2% of total prevalent ESRD, using the 2005 ADR of USRDS.

Cancer causing CKD?

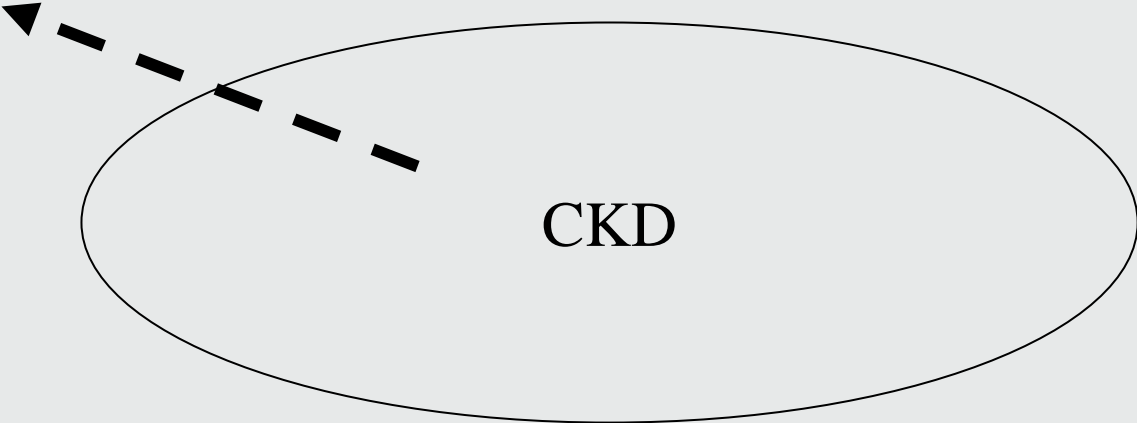
- Data from France, the IRMA study, show that over 30% of prevalent cancer patients had a GFR < 80 ml/min. (Launay-Vacher et al).
- Up to 50% of BMT/HSCT survivors may have CKD
- Late effects of cancer treatment are generally not well-known, and modest azotemia may seem unimportant to the cured cancer patient

Cancer causing ESRD: a broader view

- Cancer and its treatment in subjects with CKD: largely unstudied
- Most cancer drug trials exclude subjects with CKD
- It is possible that some CKD subjects have progression to ESRD because of cancer and its treatment

- Cancer could cause ESRD
- Cancer could cause CKD
- CKD could cause cancer
- Treatment of CKD could cause cancer

Cancer



CKD

Some cancers are increased in ESRD,
and probably also in CKD

- Kidney
- Bladder
- Medullary cancer of thyroid

Age-specific incidence of kidney cancer and bladder cancer per 100,000

- Up to 100-fold increased for kidney cancer
- Ten fold increased for bladder cancer

Stewart JH, et al. JASN 14:197, 2003

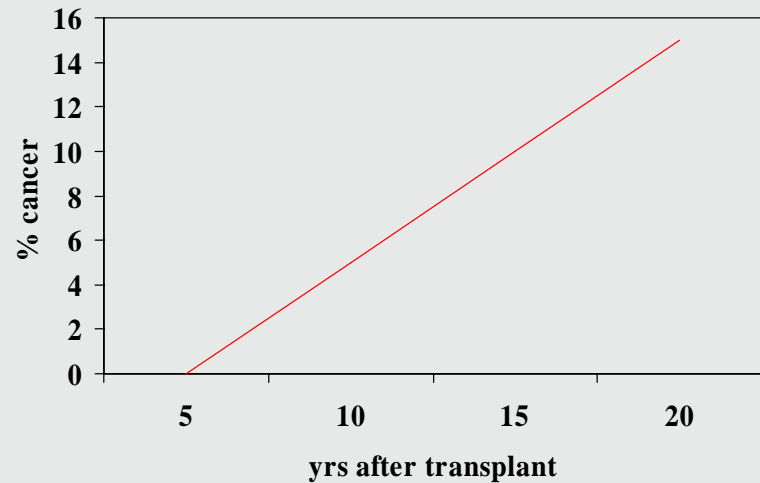
increased importance as transplant wait time increases

Evidence for CKD causing cancer

- Osaka database (Irie & Iso) suggests no excess cancer deaths in CKD population
- MDRD population had a 4% death rate from cancer (Menon), which is roughly equal to that of an age-matched population
- These two studies suggest that neither incidence of cancer nor its outcome are especially increased in CKD

Parenthesis regarding kidney transplantation

- Cancer occurrence is well-known
- Its types are different from the general population
- Immunosuppression, rather than low GFR, is the mechanism

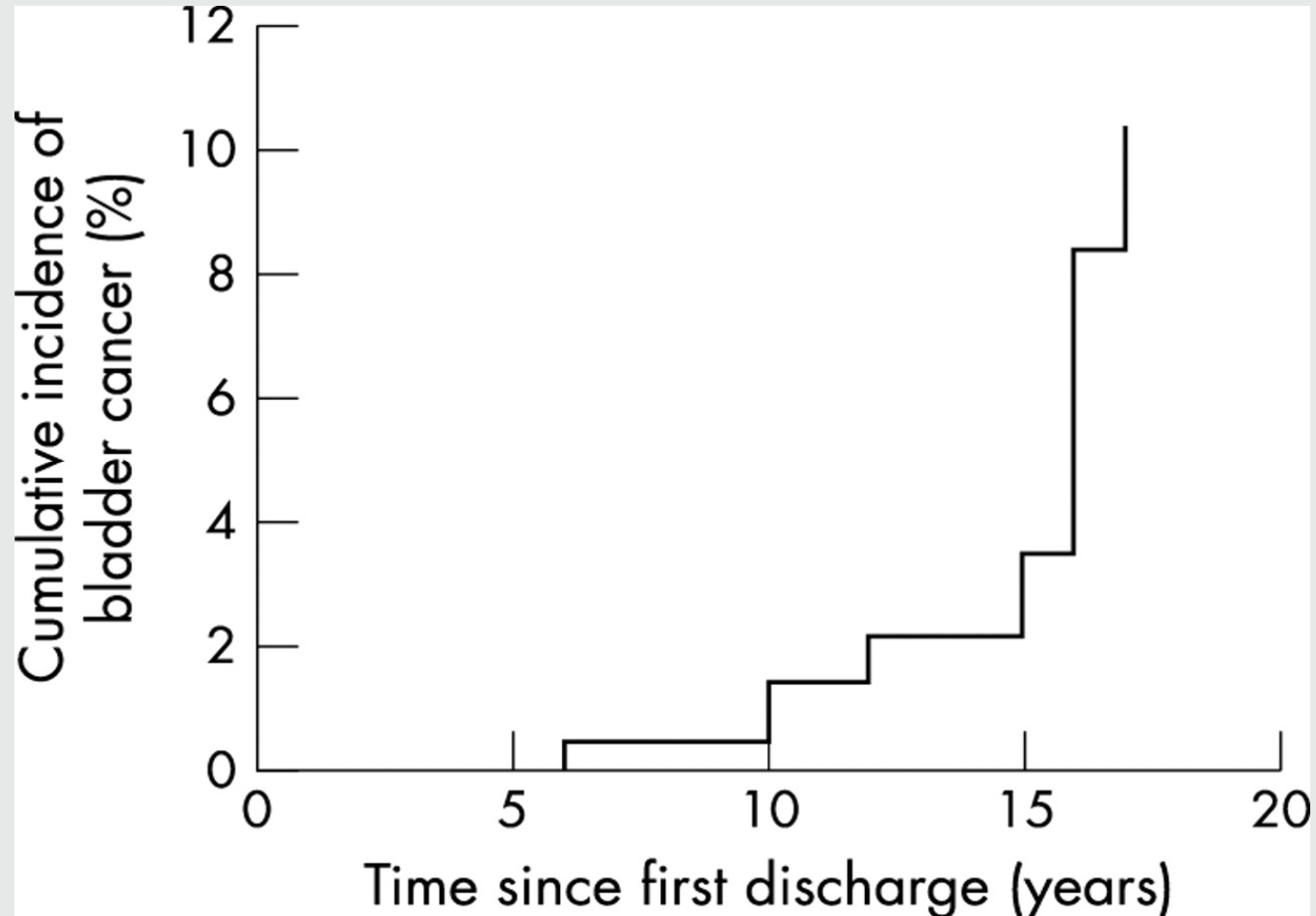


- Cancer could cause ESRD
- Cancer could cause CKD
- CKD could cause cancer
- **Treatment of CKD could cause cancer**

Treatments for CKD: a cause of cancer ?

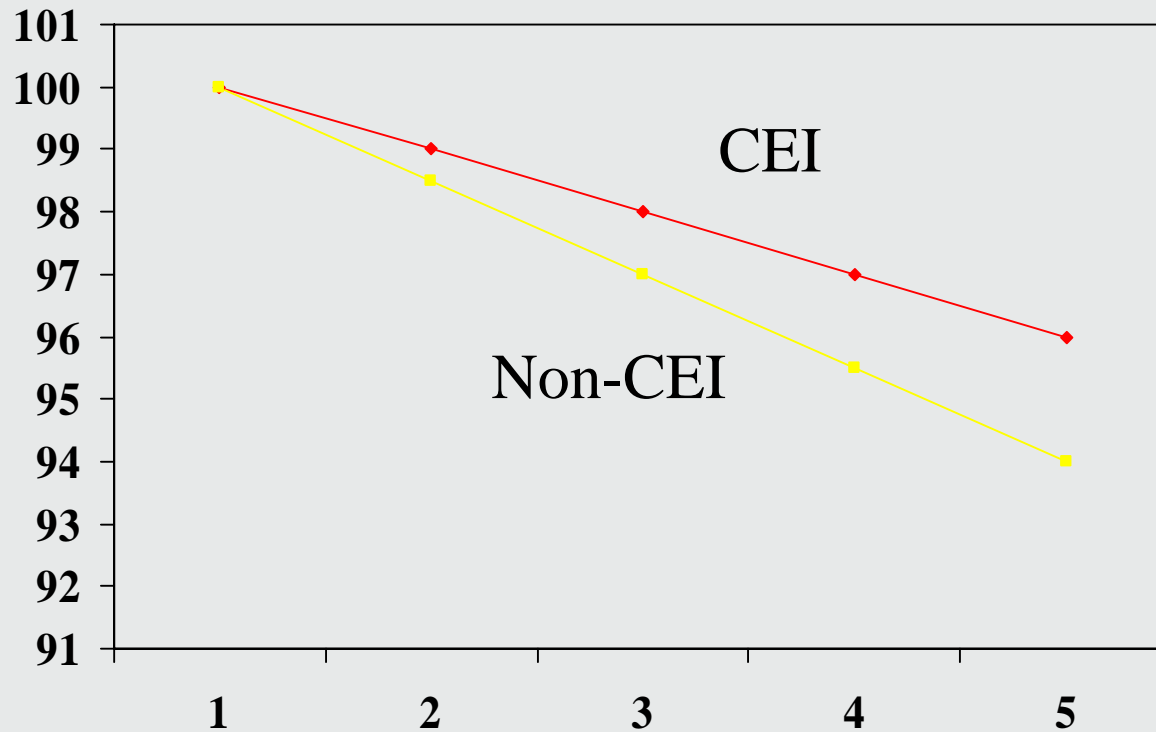
- Diuretics and kidney cancer: controversial
- Immunosuppression: limited effects
- Cyclophosphamide: definite association
- CEI: a protective effect

Cumulative incidence of bladder cancer by time since diagnosis of Wegener's granulomatosis.



Knight, A et al. Ann Rheum Dis 2004;63:1307-1311

Effect of CEI: modest but definite



Lever et al, Lancet 352:179, 1998

Effect of treatments for kidney disease

- Substantial in magnitude for cyclophosphamide but for a very limited total population
- Affecting many people for CEI but with limited absolute effect

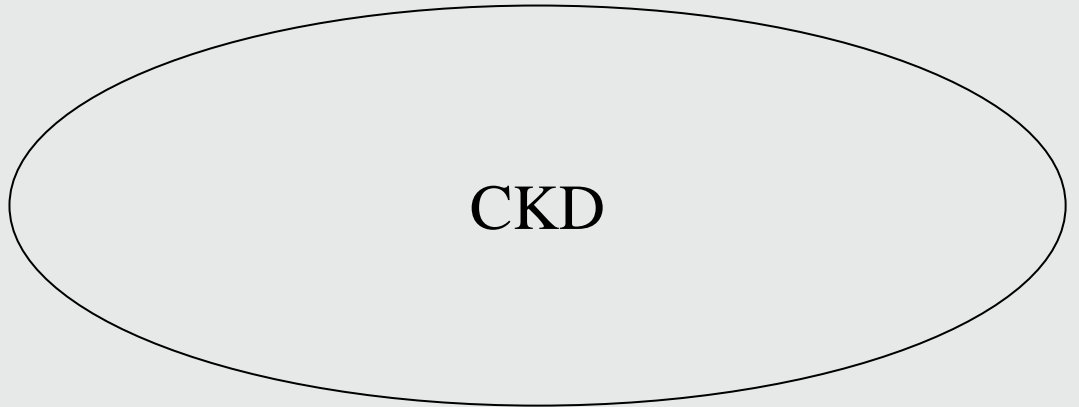
- Cancer could cause ESRD
- Cancer could cause CKD
- CKD could cause cancer
- Treatment of CKD could cause cancer

How to explain the Xue et al figure of 31% prevalent cancer at start of ESRD?

Perhaps by common risk factors

diabetes
smoking
obesity
age

Cancer

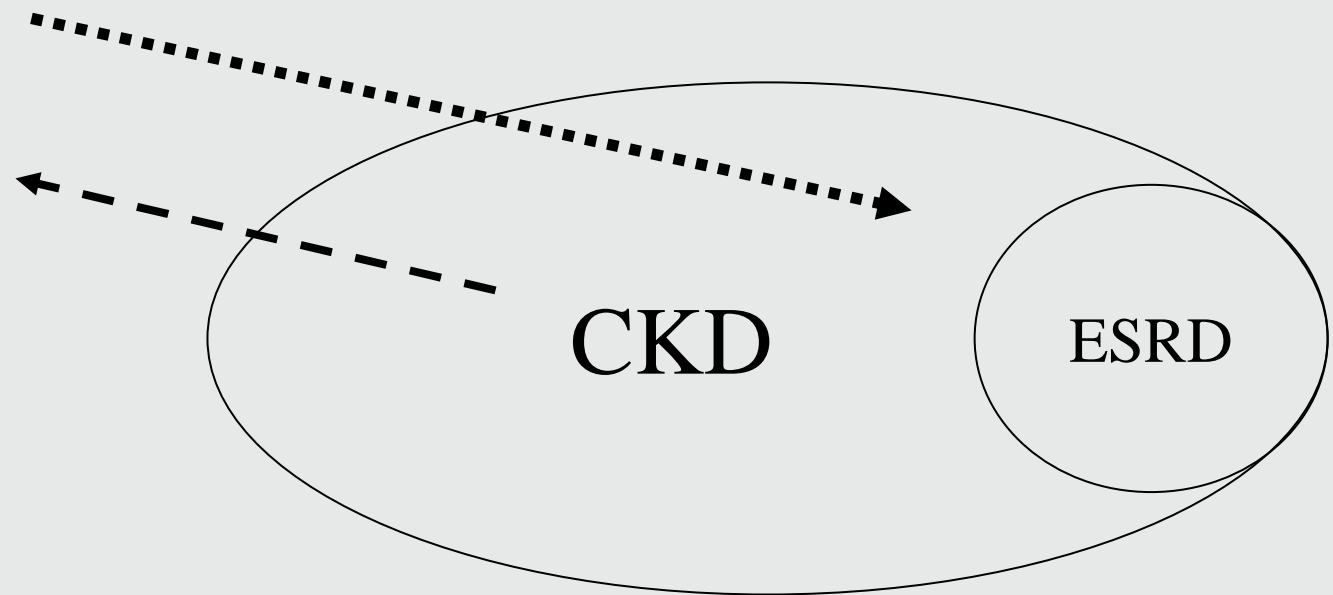


CKD

Cancer in people with CKD

- Same incidence rates as general population
- Generally excluded from planned trials
- Outcomes data not well-known

Cancer



- Cancer to ESRD is tragic but limited.
- Cancer causing un-diagnosed CKD is ill-defined and damaging.
- CKD causing cancer is definite for kidney and bladder but not for cancer in general.
- Cancer in people with CKD is not less or more frequent than in the general population.

Framework for discussion

Cancer type	CKD prevalence	CKD as a risk factor for cancer morbidity	CKD as a risk factor for cancer mortality
<i>Kidney and urinary tract tumors</i>	Yes : 1,2,3	Yes:.,2,3,4	Probable: 2,3,4
<i>Other solid tumors</i>	Possible: 5,6	Effect on chemotherapy:6,7	Association of proteinuria:8 Reduced risk, CEI:9
<i>Hematologic malignancies</i>	Unknown	Likely but unknown	Proteinuria in lymphoma:10

1. Huang, Lancet Oncol 7: 735, 2006
2. Stewart, J Am Soc Nephrol 14:197, 2003
3. Matson, Medicine 69:217, 1990
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5. Kotzmann, Thyroid. 9:943, 1999
6. Cassidy, Ann Oncol 13:566, 2002
7. Jodrell, J Clin Oncol 10:520, 1992
8. Pedersen, Eur J Cancer 34:76, 1998
9. Lever, Lancet 352, 179, 1998
10. Pedersen, Scand J Clin Lab Invest 65:477, 2005

My choices for priorities

- CKD after cancer cure: identification, effect on life quality and quantity
- Outcomes in CKD patients who have cancer: definition and analysis

Thank you for your attention

Parenthesis regarding screening

If cancer occurrence is not increased in people with CKD then routine cancer screening is not indicated.

That's because of the competing risks of CV disease.

Graph adapted from Go et al, NEJM 351:1296, 2004

