

Supplemental Material

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Supplemental Table 1: Actual Search Strategies

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Database(s): Ovid MEDLINE(R) 1946 to Present and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) Daily, EBM Reviews - Cochrane Central Register of Controlled Trials November 2021, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to December 28, 2021, Embase 1974 to 2021
December 30

Search Strategy:

#	Searches
1	exp Acute Kidney Injury/ or acute kidney failure/
2	(acute adj2 ("kidney injury" or "kidney failure" or "kidney insufficiency" or "renal injury" or "renal failure" or "renal insufficiency")).ti,ab,hw,kw.
3	1 or 2
4	exp Sodium/
5	((("fractional excretion" or "excreted fraction*") adj5 (sodium or natrium or na)) or ("fena" or fena)).ti,ab,hw,kw.
6	4 or 5
7	3 and 6
8	(exp animals/ or exp nonhuman/) not exp humans/
9	((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) not (human or humans or patient or patients)).ti,ab,hw,kw.
10	(rat or rats or mice or mouse or murine or pig or pigs or porcine or swine or dog or dogs).ti.
11	or/8-10
12	7 not 11
13	limit 12 to english language [Limit not valid in CDSR; records were retained]
14	limit 12 to no language specified [Limit not valid in CDSR; records were retained]
15	13 or 14
16	remove duplicates from 15

SCOPUS

1	TITLE-ABS-KEY (acute W/2 ("kidney injury" or "kidney failure" or "kidney insufficiency" or "renal injury" or "renal failure" or "renal insufficiency"))
2	TITLE-ABS-KEY (((("fractional excretion" or "excreted fraction*") W/5 (sodium or natrium or na)) or ("fena" or fena))
3	1 and 2
4	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*)
5	3 not 4
6	DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh) OR DOCTYPE(ch)
7	5 not 6
8	LANGUAGE(english)
9	7 and 8
10	(TITLE-ABS-KEY ((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR

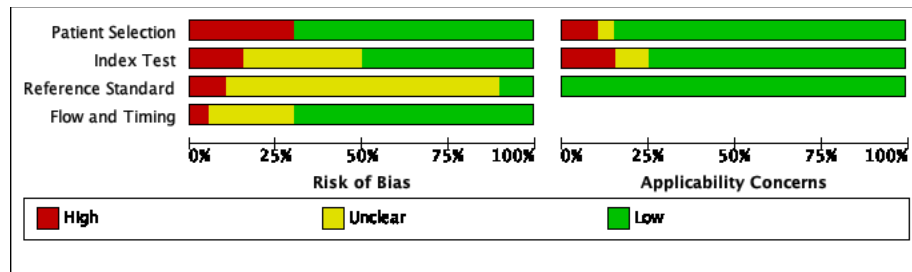
	<p> baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze 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))) </p>
11	9 not 10

Supplemental Table 2: QUADAS-2 classification

Domain 1: Patient selection	Patient sampling	Patients who developed AKI, defined by any known criteria or equivalent, and have had a FENa test.
	Was a consecutive or random sample of patients enrolled?	Yes: if a consecutive or random sample of participants were enrolled. No: if a consecutive or random sample of participants were not enrolled. Unclear: if the study does not describe the method of participants enrolment.
	Was a case-control design avoided?	Yes: if the study has not used a case-control design. No: if the study has used a case-control design. Unclear: if the study does not report enough information to fulfill whether a case-control design was used.
	Did the study avoid inappropriate exclusions?	Yes: if the study has included the results of all patients in the study irrespective of their comorbidities or characteristics. No: if the study has excluded patients from the analysis based on having factors that may affect the test result Unclear: if the study does not report enough information.
	Could the selection of patients have introduced bias?	Low risk of bias: if 'yes' was the answer for all of the above 3 questions. High risk of bias: if 'no' was the answer for any of the above 3 questions. Unclear risk of bias: if 'unclear' was the answer for any of the above 3 questions but without a 'no' answer for any of the above 3 questions.
	Patient characteristics and setting	Patients' settings for each study will be listed under "Patient characteristics and setting" in the table of "Characteristics of included studies".
	Are there concerns that the included patients and setting do not match the review question?	Low, high, or unclear concern were returned for the applicability based on the answer for the third signaling question above and on balancing how closely the sample meets the target population of interest.
Domain 2: Index tests	Index test	Fractional Excretion of Sodium (FENa)
	Were the index test results interpreted without knowledge of the results of the reference standard?	Yes: if the report stated that the person undertaking the index test did not know the results of the reference tests or if the index test appeared to be carried out before the reference standard. No: if the report stated that the same person conducted both tests or that the results of the index test were known to the person undertaking the reference tests. Unclear: if insufficient information is provided.
	If a threshold was used, was it pre-specified?	Yes: if prespecified No: if the authors selected the best non-prespecified cut-off value based on the results of the study. Unclear: if there is doubt which cut-off has been used.
	Could the conduct or interpretation of the index test have introduced bias?	Low risk of bias: if 'yes' was the answer for both of the above questions. High risk of bias: if 'no' was the answer for any of the above 2 questions. Unclear risk of bias: if 'unclear' was the answer for any of the above 2 questions but without a 'no' answer for any of the above 2 questions.
	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	An answer of low, high, or unclear concern about applicability will be made based on a balanced assessment of the information reported under domain 2 'Index test'
Domain 3: Target condition and reference standard	Target condition and reference standard(s)	Target condition: AKI defined by any known criteria or their equivalent. The information for the reference standard is reported under 'Reference standard(s)' in the 'Characteristics of included studies'

	Are the reference standards likely to correctly classify the target condition?	Yes: if reference standard is one of the following: (1) responsiveness to volume expansion; (2) kidney biopsy, with or without microscopic analysis of the urine No: if the reference standard was none of the above Unclear: if the information is insufficient.
	Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes: if the reference standard was interpreted without the knowledge of the results of the index test. No: if the reference standard was interpreted with the knowledge of the results of the index test. Unclear: it is not clear whether the reference standard was interpreted without the knowledge of the results of the index test.
	Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk of bias: if 'yes' was the answer for both of the above 2 questions. High risk of bias: if 'no' was the answer for any of the above 2 questions. Unclear risk of bias: if 'unclear' was the answer for any of the above 2 questions but without a 'no' answer for any of the above 2 questions.
	Are there concerns that the target condition as defined by the reference standard does not match the question?	The answer to this question will always be "No concern" because if they did not match, the study will be excluded.
Domain 4: Flow and timing	Flow and timing	Patients may have progression of the disease from prerenal into intrinsic renal AKI, or they may spontaneously recover. The reference standards should be carried within 2 to 3 days.
	Was there an appropriate interval between index test and reference standard?	Yes: if the time interval between the index test and the reference standard was less than 3 days. No: if the time interval between the index test and the reference standard was more than 3 days. Unclear: if the time interval between the index test and the reference standard was unclear.
	Did all patients receive the same reference standard?	Yes: if all the patients received the same reference standard. No: if different patients received different reference standards. Unclear: if it was not clear whether the patients received the same reference standard or did not.
	Could the patient flow have introduced bias?	Low risk of bias: if 'yes' was the answer for both of the above 2 questions. High risk of bias: if 'no' was the answer for any of the above 2 questions. Unclear risk of bias: if 'unclear' was the answer for any of the above 2 questions but without a 'no' answer for any of the above 2 questions.

Supplemental figure 1-a: Risk of bias and applicability concerns graph



Description: Review authors' judgements about each domain presented as percentages across included studies. (*Output from Review Manager (RevMan) [Computer program]*).

Supplemental figure 1-b: Risk of bias and applicability concerns summary

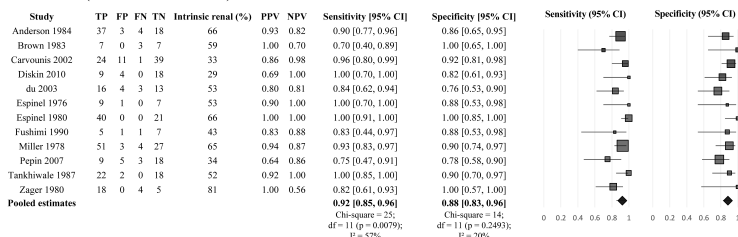
	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Anderson 1984	+	+	?	+	+	+	+
Brown 1983	+	?	?	?	+	+	+
Carvounis 2002	+	?	+	?	+	+	+
Chugh 1981	+	?	?	?	+	+	+
Darmon 2011	+	+	?	+	+	+	+
Dewitte 2012	+	+	?	+	+	+	+
Diskin 2010	+	+	?	+	+	+	+
du 2003	+	?	+	+	+	+	+
Espinel 1976	+	+	?	+	?	+	+
Espinel 1980	+	+	+	+	+	+	+
Fushimi 1990	+	?	?	+	+	+	+
Gowda (D) 2021	+	+	?	+	+	+	+
Gowda (V) 2021	+	+	?	+	+	+	+
Miller 1978	+	+	?	+	+	+	+
Patidar 2017	+	+	?	+	+	?	+
Pepin 2007	+	+	+	+	+	+	+
Steinhauslin 1994	+	+	?	+	+	+	+
Tankhwal 1987	+	?	?	?	+	+	+
Yassin 2013	+	?	?	?	+	?	+
Zager 1980	+	+	?	+	+	+	+

High
 Unclear
 Low

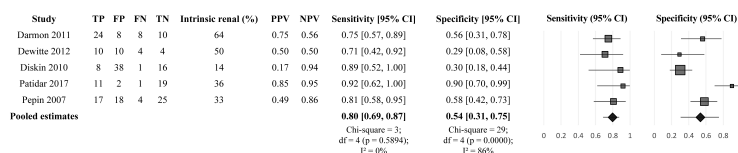
Description: Review authors' judgements about each domain for each included study. (Output from Review Manager (RevMan) [Computer program])

Supplemental figure 2: Forest plots for the subgroup analysis

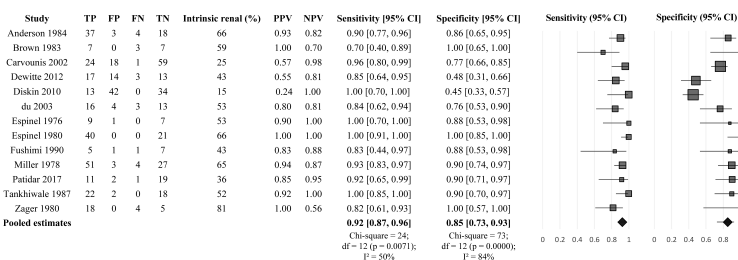
1- FENa 1% (Patients not on diuretics)



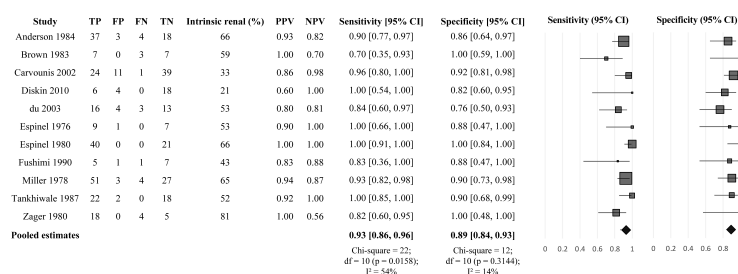
2- FENa 1% (Patients on diuretics)



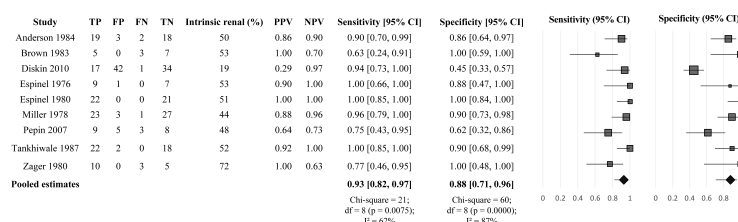
3- FENa 1% (Without CKD patients)



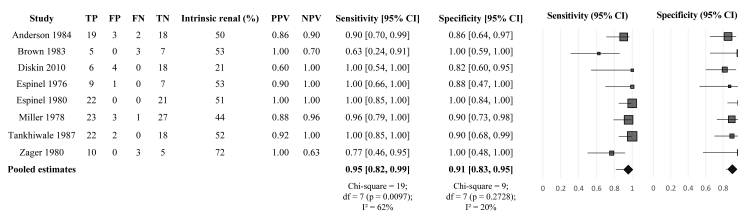
4- FENa 1% (Patients without CKD and not on diuretics)



5- FENa 1% (Oliguric patients)

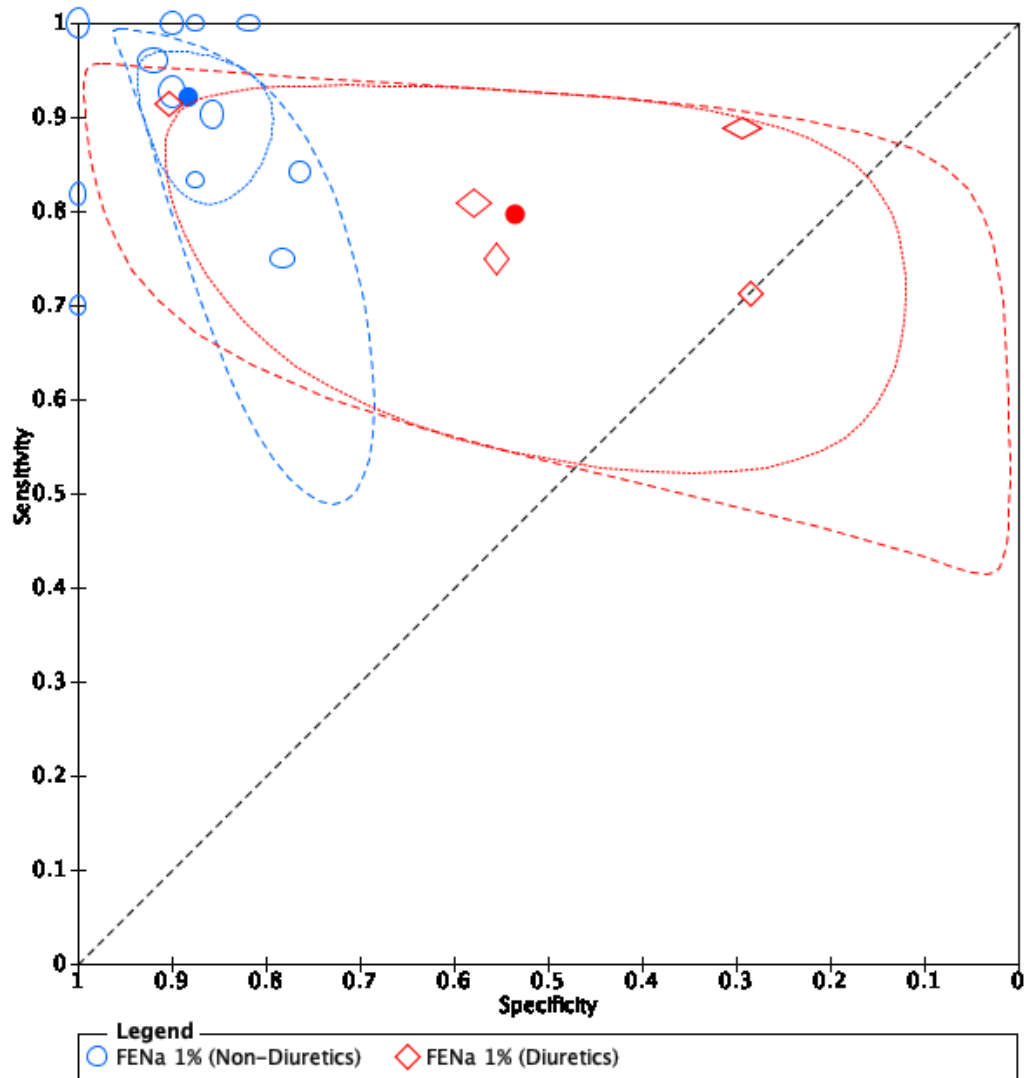


6- FENa 1% (Oliguric patients without CKD and not on diuretics)



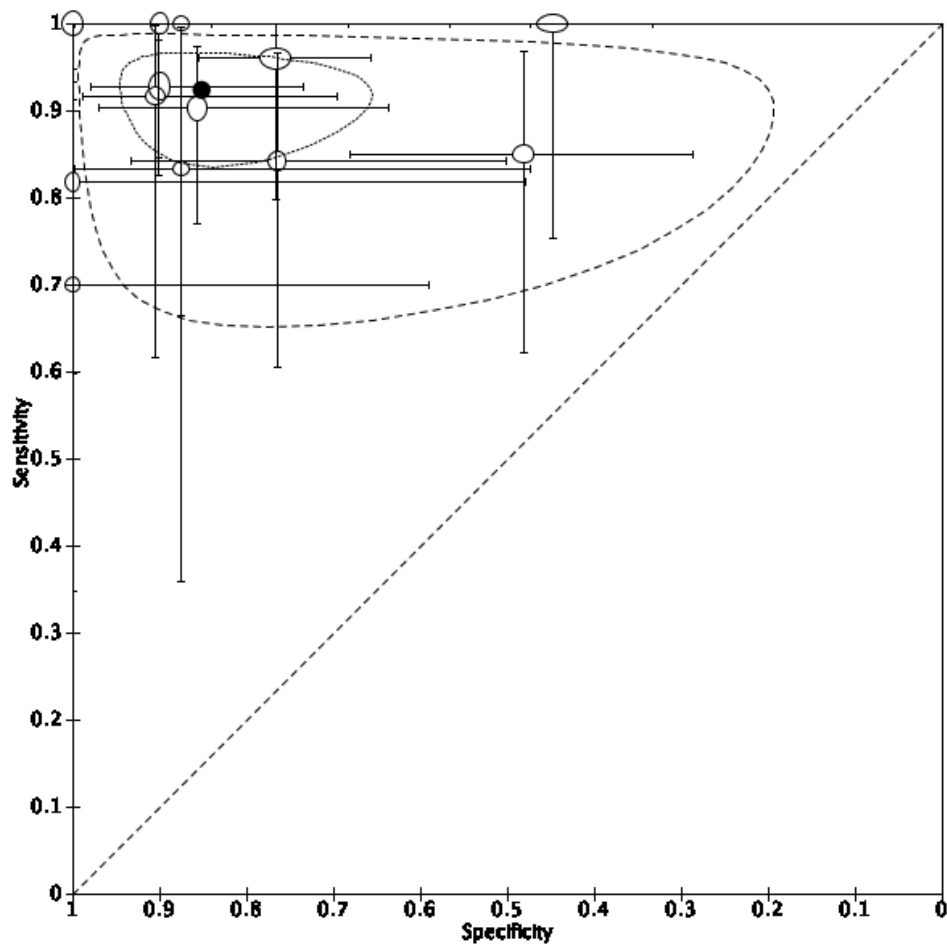
Description: The size of the square is proportional to the size of the population. The diamond represents the pooled estimates. TP: True Positive, FP: False Positive, FN: False Negative, TN: True Negative, PPV: Positive Predictive Value, NPV: Negative Predictive Value.

Supplemental figure 3-a: Summary receiver operating characteristic plot for the non-diuretics and diuretics subgroups



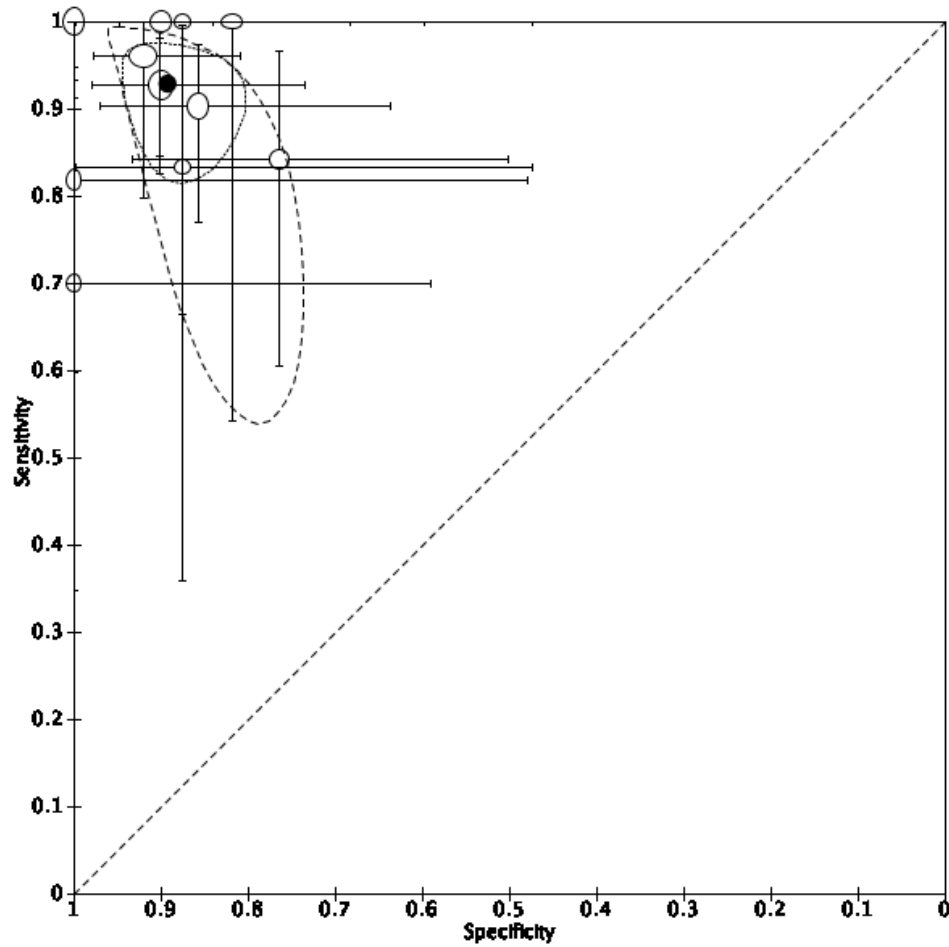
Description: The summary operating point (the filled circles) with the estimated average sensitivities and specificities with their 95% confidence (dotted curve) and prediction regions (dashed curve) for the non-diuretics subgroup (blue) compared to the diuretics subgroup (red). The size of the ellipsoid and diamond are proportional to the sample size for each study. (Output from Review Manager (RevMan) [Computer program])

Supplemental figure 3-b: Summary receiver operating characteristic plot for the 13 studies that excluded chronic kidney disease patients



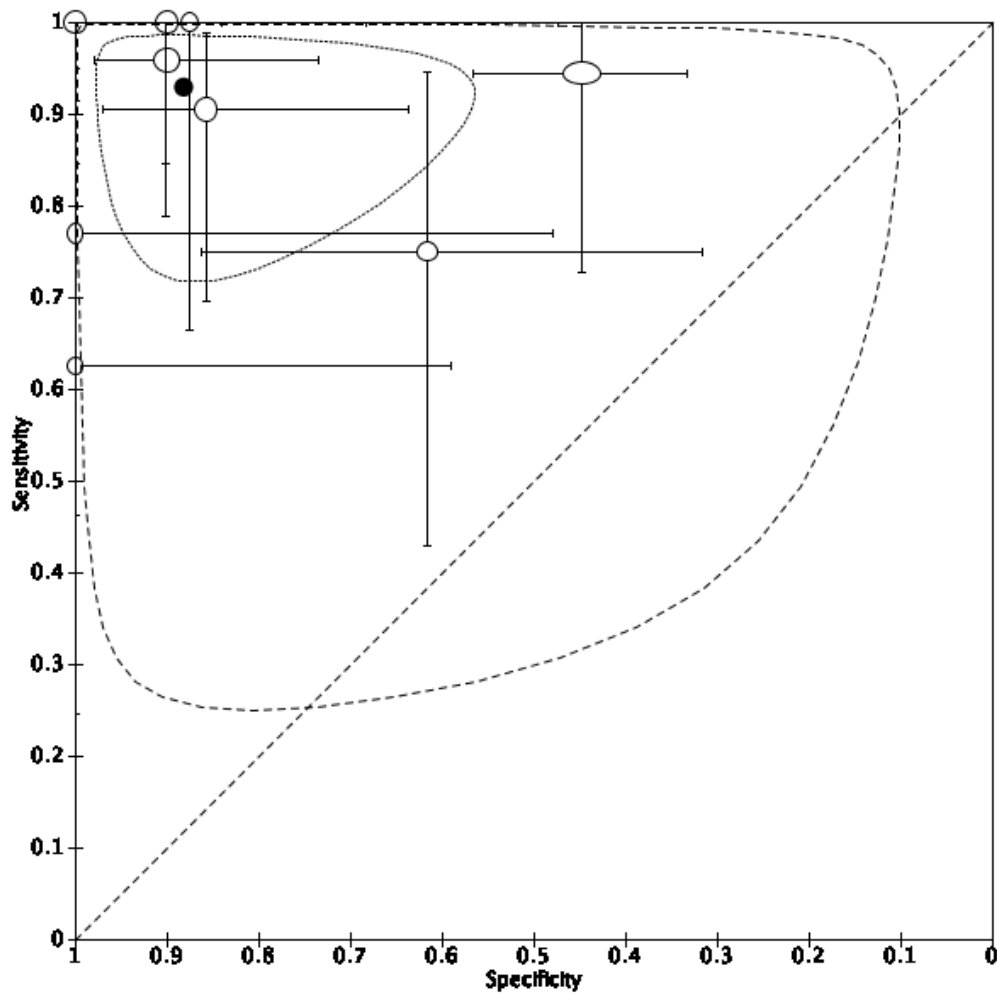
Description: The summary operating point (the filled circle) with the estimated average sensitivities and specificities with their 95% confidence (dotted curve) and prediction regions (dashed curve) for the 13 studies that excluded CKD patients. The size of the ellipsoid is proportional to the sample size for each study. (Output from Review Manager (RevMan) [Computer program])

Supplemental figure 3-c: Summary receiver operating characteristic plot for the 11 studies that excluded chronic kidney disease and diuretics patients



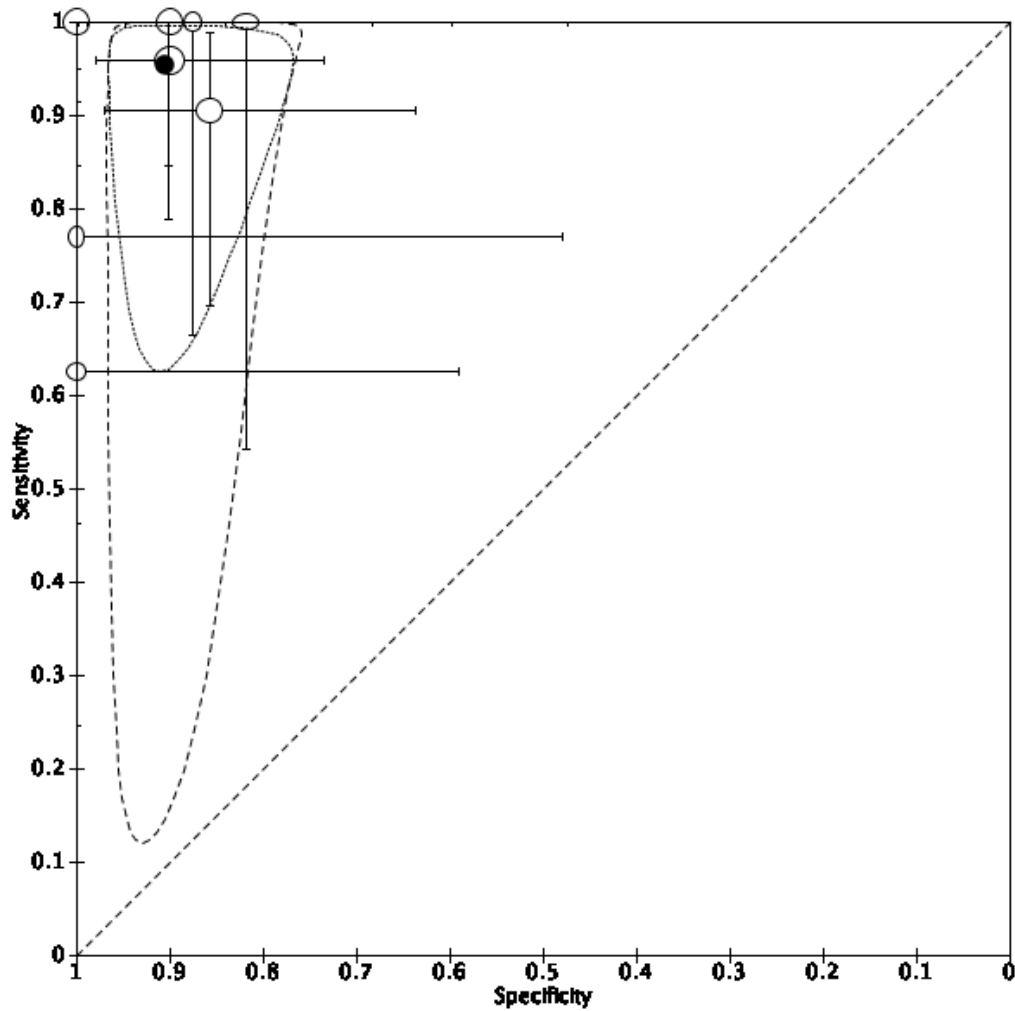
Description: The summary operating point (the filled circle) with the estimated average sensitivities and specificities with their 95% confidence (dotted curve) and prediction regions (dashed curve) for the 11 studies that excluded CKD and diuretics patients. The size of the ellipsoid is proportional to the sample size for each study. (Output from Review Manager (RevMan) [Computer program])

Supplemental figure 3-d: Summary receiver operating characteristic plot for the 9 studies included in the oliguric subgroup analysis



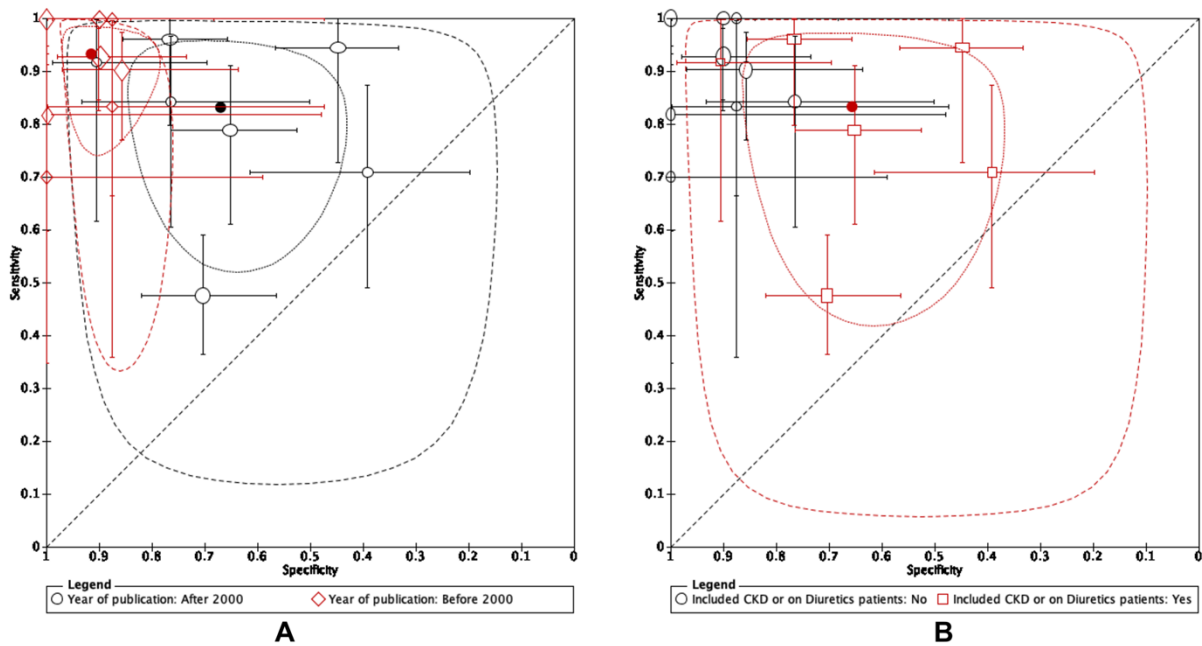
Description: The summary operating point (the filled circle) with the estimated average sensitivities and specificities with their 95% confidence (dotted curve) and prediction regions (dashed curve) for the 9 studies included in the oliguric subgroup analysis. The size of the ellipsoid is proportional to the sample size for each study. (Output from Review Manager (RevMan) [Computer program])

Supplemental figure 3-e: Summary receiver operating characteristic plot for the 7 studies that included oliguric patients with no history of CKD or diuretics intake.



Description: The summary operating point (the filled circle) with the estimated average sensitivities and specificities with their 95% confidence (dotted curve) and prediction regions (dashed curve) for the 7 studies that included oliguric patients with no history of CKD or diuretics intake. The size of the ellipsoid is proportional to the sample size for each study. (Output from Review Manager (RevMan) [Computer program])

Supplemental figure 3-f: Summary receiver operating characteristic plot for the 15 studies used fractional excretion of sodium at 1% threshold



Description: The summary operating point (the filled circles) with the estimated average sensitivities and specificities with their 95% confidence (dotted curve) and prediction regions (dashed curve) for A: comparison between the recent (black) and the older (red) subgroups, B (red): studies that included CKD or diuretics patients. (Output from Review Manager (RevMan) [Computer program])