Supplementary Material

Figure S1. Funnel plot of the studies included in the all-cause mortality meta-analysis.

Funnel plot of standard error by log hazard ratio for all-cause mortality for the studies included in the meta-analysis.

Figure S2. Sensitivity analyses of meta-analysis of all-cause mortality

Legend: Pooled hazard ratio for long-term all-cause mortality in solid organ transplant recipients with pre-transplant malignancies compared to recipients without pre-transplant malignancies using a random effects model and (A) removing the estimated HR, (B) removing unadjusted hazard ratio estimates or removing non-population based studies (as only population-based studies reported adjusted hazard ratios, only one forest plot is presented), and (C) removing studies with unknown length of follow-up. For Santos 2014 a and b refer to two different non-overlapping studies by the same author and published the same year. For b the number of patients with and without PTM was not presented.

Abbreviations: PTM: Pre-transplant malignancy | SE: Standard error | IV: Inverse variance | CI: Confidence interval | N/A: Not available

Figure S3. Subgroup meta-analysis of all-cause mortality by transplanted organ

Legend: Pooled hazard ratio for long-term all-cause mortality in solid organ transplant recipients with pre-transplant malignancies compared to recipients without pre-transplant malignancies using a random effects model stratified by (A) kidney recipients and (B) non-kidney recipients. For Santos 2014 *a* and *b* refer to two different non-overlapping studies by the same author and published the same year. For *b* the number of patients with and without PTM was not presented.

Abbreviations: PTM: Pre-transplant malignancy | SE: Standard error | IV: Inverse variance | CI: Confidence interval | N/A: Not available

Figure S4. Sensitivity analyses of meta-analysis of incidence of post-transplant *de novo* malignancy

Legend: Pooled hazard ratio for incidence of post-transplant de novo malignancy in solid organ transplant recipients with pre-transplant malignancies compared to recipients without pre-transplant malignancies: (A) removing the estimated hazard rations from the incidence rate ratios and (B) excluding unadjusted estimates.

Abbreviations: PTM: Pre-transplant malignancy | SE: Standard error | IV: Inverse variance | CI: Confidence interval | N/A: Not available

Figure S5. Subgroup meta-analysis of incidence of post-transplant *de novo* malignancy by transplanted organ

Legend: Pooled hazard ratio for incidence of post-transplant *de novo* malignancy in (A) kidney transplant recipients and (B) non-kidney transplant recipients with pre-transplant malignancies compared to kidney recipients without pre-transplant malignancies.

Figure S6. Sensitivity analysis of meta-analysis of NMSC post-transplant de novo malignancy incidence.

Legend: Pooled hazard ratio for incidence of post-transplant *de novo* non-melanoma skin cancer in solid organ transplant recipients with pre-transplant malignancies compared to recipients without pre-transplant malignancies using a random effects model and removing the study by Esfeh *et al*.

Abbreviations: PTM: Pre-transplant Malignancy | NMSC: Non-melanoma skin cancer | SE: Standard error | IV: Inverse variance | CI: Confidence interval

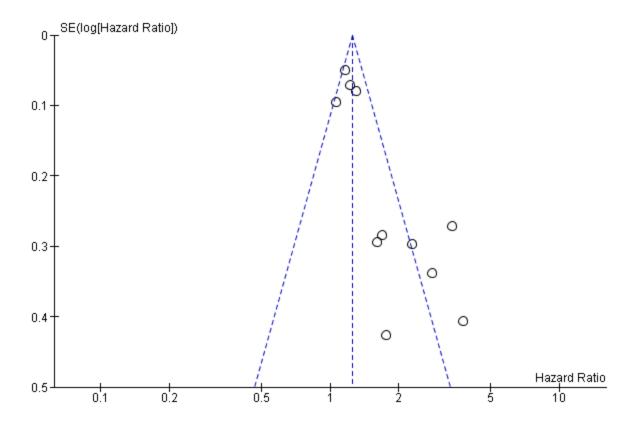


Figure S1. Funnel plot of the studies included in the all-cause mortality meta-analysis. Funnel plot of standard error by log hazard ratio for all-cause mortality for the studies included in the meta-analysis.

Figure S2. Sensitivity analyses of meta-analysis of all-cause mortality

			PTM	Non-PTM		Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Cortazar 2012	1.335	0.4057	35	958	4.0%	3.80 [1.72, 8.42]	
Farrugia 2014	0.8198	0.2963	74	19029	6.5%	2.27 [1.27, 4.06]	 -
Tovikkai 2015	0.47	0.2936	64	3773	6.6%	1.60 [0.90, 2.84]	+-
Chung 2014	1.2238	0.2707	31	1925	7.4%	3.40 [2.00, 5.78]	
Beaty 2013	0.0583	0.095	1857	31573	17.5%	1.06 [0.88, 1.28]	+
Brattstrom 2014	0.2624	0.0797	416	10032	18.6%	1.30 [1.11, 1.52]	
Santos 2014(a)	0.1989	0.0717	1128	5635	19.1%	1.22 [1.06, 1.40]	-
Santos 2014(b)	0.1484	0.0508	0	0	20.3%	1.16 [1.05, 1.28]	-
Total (95% CI)			3605	72925	100.0%	1.43 [1.20, 1.70]	•
Heterogeneity: Tau² = Test for overall effect:		0.1 0.2 0.5 1 2 5 10 Favours PTM Favours non-PTM					

В

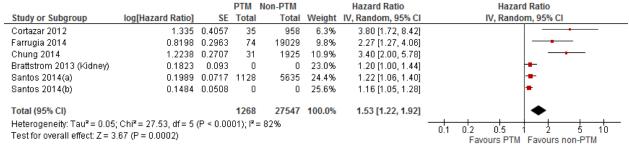
			PTM	Non-PTM		Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Farrugia 2014	0.8198	0.2963	74	19029	5.9%	2.27 [1.27, 4.06]	
Tovikkai 2015	0.47	0.2936	64	3773	5.9%	1.60 [0.90, 2.84]	+
Chung 2014	1.2238	0.2707	31	1925	6.7%	3.40 [2.00, 5.78]	
Beaty 2013	0.0583	0.095	1857	31573	18.5%	1.06 [0.88, 1.28]	+
Brattstrom 2014	0.2624	0.0797	416	10032	19.9%	1.30 [1.11, 1.52]	-
Santos 2014(a)	0.1989	0.0717	1128	5635	20.7%	1.22 [1.06, 1.40]	-
Santos 2014(b)	0.1484	0.0508	0	0	22.4%	1.16 [1.05, 1.28]	-
Total (95% CI)			3570	71967	100.0%	1.34 [1.14, 1.58]	•
	= 0.03; Chi² = 23.39, d : Z = 3.60 (P = 0.0003	0.1 0.2 0.5 1 2 5 10 Favours PTM Favours non-PTM					

C

			PTM	Non-PTM		Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Ladowski 2006	0.5596	0.4255	13	201	8.9%	1.75 [0.76, 4.03]	
Cortazar 2012	1.335	0.4057	35	958	9.3%	3.80 [1.72, 8.42]	
Koerner 1997	1.026	0.3375	20	682	11.2%	2.79 [1.44, 5.41]	_
Farrugia 2014	0.8198	0.2963	74	19029	12.5%	2.27 [1.27, 4.06]	
Tovikkai 2015	0.47	0.2936	64	3773	12.6%	1.60 [0.90, 2.84]	 •
Fernandez 2010	0.5247	0.2833	12	583	12.9%	1.69 [0.97, 2.94]	-
Chung 2014	1.2238	0.2707	31	1925	13.3%	3.40 [2.00, 5.78]	
Brattstrom 2014	0.2624	0.0797	416	10032	19.4%	1.30 [1.11, 1.52]	
Total (95% CI)			665	37183	100.0%	2.08 [1.49, 2.89]	•
Heterogeneity: Tau² = Test for overall effect:		0.1 0.2 0.5 1 2 5 10					
restroi overali ellect.	Z = 4.34 (F % 0.000)	Favours PTM Favours non-PTM					

Legend: Pooled hazard ratio for long-term all-cause mortality in solid organ transplant recipients with pre-transplant malignancies compared to recipients without pre-transplant malignancies using a random effects model and (A) removing the estimated HR, (B) removing unadjusted hazard ratio estimates or removing non-population based studies (as only population-based studies reported adjusted hazard ratios, only one forest plot is presented), and (C) removing studies with unknown length of follow-up. For Santos 2014 a and b refer to two different non-overlapping studies by the same author and published the same year. For b the number of patients with and without PTM was not presented.

Figure S3. Subgroup meta-analysis of all-cause mortality by transplanted organ

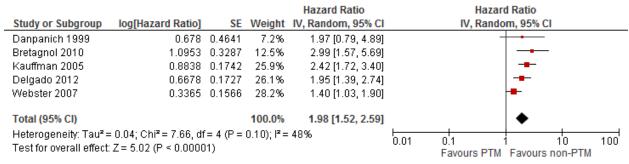


В

		P	PTM I	Non-PTM		Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE 7	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Ladowski 2006	0.5596 0	.4255	13	201	9.7%	1.75 [0.76, 4.03]	
Koerner 1997	1.026 0	.3375	20	682	12.8%	2.79 [1.44, 5.41]	
Tovikkai 2015	0.47 0	0.2936	64	3773	14.7%	1.60 [0.90, 2.84]	 •
Fernandez 2010	0.5247 0	0.2833	12	583	15.2%	1.69 [0.97, 2.94]	-
Brattstrom 2013 (Non-Kidney)	0.5878	0.166	0	0	21.8%	1.80 [1.30, 2.49]	-
Beaty 2013	0.0583	0.095	1857	31573	25.8%	1.06 [0.88, 1.28]	*
Total (95% CI)		•	1966	36812	100.0%	1.61 [1.17, 2.22]	•
Heterogeneity: Tau² = 0.09; Chi² = 15.37, df = 5 (P = 0.009); i² = 67% Test for overall effect: Z = 2.93 (P = 0.003)							0.1 0.2 0.5 1 2 5 10 Favours PTM Favours non-PTM

Legend: Pooled hazard ratio for long-term all-cause mortality in solid organ transplant recipients with pre-transplant malignancies compared to recipients without pre-transplant malignancies using a random effects model stratified by (A) kidney recipients and (B) non-kidney recipients. For Santos 2014 a and b refer to two different non-overlapping studies by the same author and published the same year. For b the number of patients with and without PTM was not presented.

Figure S4. Sensitivity analyses of meta-analysis of incidence of post-transplant *de novo* malignancy



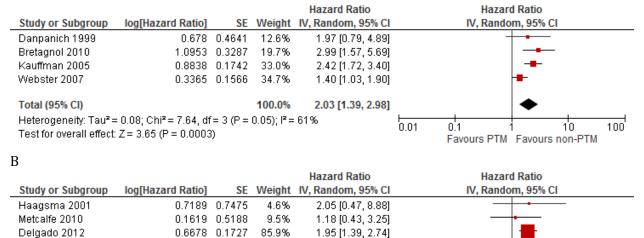
В

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI		Hazard Ratio IV, Random, 95% CI
Bretagnol 2010	1.0953	0.3287	14.6%	2.99 [1.57, 5.69]		-
Kauffman 2005	0.8838	0.1742	27.7%	2.42 [1.72, 3.40]		
Delgado 2012	0.6678	0.1727	27.9%	1.95 [1.39, 2.74]		-
Webster 2007	0.3365	0.1566	29.7%	1.40 [1.03, 1.90]		-
Total (95% CI)			100.0%	2.00 [1.47, 2.71]		•
Heterogeneity: Tau ² =		0.01	0.1 1 10 100			
Test for overall effect:	Z = 4.40 (P < 0.0000		Favours PTM Favours non-PTM			

Legend: Pooled hazard ratio for incidence of post-transplant de novo malignancy in solid organ transplant recipients with pre-transplant malignancies compared to recipients without pre-transplant malignancies: (A) removing the estimated hazard rations from the incidence rate ratios and (B) excluding unadjusted estimates.

Figure S5. Subgroup meta-analysis of incidence of post-transplant *de novo* malignancy by transplanted organ

Total (95% CI)



Legend: Pooled hazard ratio for incidence of post-transplant de novo malignancy in (A) kidney transplant recipients and (B) non-kidney transplant recipients with pre-transplant malignancies compared to kidney recipients without pre-transplant malignancies.

1.86 [1.36, 2.55]

0.01

0.1

10

Favours PTM Favours non-PTM

100

100.0%

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.87$, df = 2 (P = 0.65); $I^2 = 0\%$

Test for overall effect: Z = 3.89 (P = 0.0001)

Figure S6. Sensitivity analysis of meta-analysis of NMSC post-transplant de novo malignancy incidence.

			PTM	Non-PTM		Hazard Ratio		Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI
Spanogle 2012	1.6014	0.4867	0	0	11.9%	4.96 [1.91, 12.88]		
Kauffman 2005	0.8416	0.4609	881	32438	13.1%	2.32 [0.94, 5.73]		 •
Rashtak 2015	1.9445	0.4454	13	153	13.9%	6.99 [2.92, 16.73]		
Alam 2011	1.0647	0.3236	0	0	23.4%	2.90 [1.54, 5.47]		
Bretagnol 2010	0.9969	0.229	40	979	37.7%	2.71 [1.73, 4.24]		
Total (95% CI)			934	33570	100.0%	3.31 [2.33, 4.70]		•
Heterogeneity: Tau² =	0.03; Chi² = 4.99, df		0.01	0.1 10 100				
Test for overall effect:	Z = 6.67 (P < 0.0000)		0.01	Favours [PTM] Favours [non-PTM]				

Legend: Pooled hazard ratio for incidence of post-transplant *de novo* non-melanoma skin cancer in solid organ transplant recipients with pre-transplant malignancies compared to recipients without pre-transplant malignancies using a random effects model and removing the study by Esfeh *et al*.

Abbreviations: PTM: Pre-transplant Malignancy | NMSC: Non-melanoma skin cancer | SE: Standard error | IV: Inverse variance | CI: Confidence interval

Appendices

Appendix 1. Literature search strategy

Appendix 2. List of sources included in the grey literature search

Appendix 3. Modified New-Castle Ottawa Coding Manual for Cohort Studies

Appendix 1. Literature search strategy

MEDLINE search strategy

- 1. exp Neoplasms/
- 2. neoplas*.tw.
- 3. cancer*.tw.
- 4. (tumour* or tumor*).tw.
- 5. malignan*.tw.
- 6. (oncology or oncologic or oncologist*).tw.
- 7. metasta*.tw.
- 8. carcinoma*.tw.
- 9. adenocarcinoma*.tw.
- 10. melanoma*.tw.
- 11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
- 12. Organ Transplantation/
- 13. exp Heart Transplantation/
- 14. Kidney Transplantation/
- 15. Liver Transplantation/
- 16. exp Lung Transplantation/
- 17. Pancreas Transplantation/
- 18. ((organ or heart or heart-lung or kidney or renal or liver or lung or pancreas) adj2 transplant*).tw.
- 19. 12 or 13 or 14 or 15 or 16 or 17 or 18
- 20. ((preexisting or pre-existing) adj5 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 21. (antecedent adj6 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 22. (history adj6 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 23. 20 or 21 or 22
- 24. 19 and 23
- 25. pretransplant*.tw.
- 26. pre-transplant*.tw.
- 27. (prior adj5 transplant*).tw.
- 28. pre-HT.tw.
- 29. pre-KT.tw.
- 30. pre-LT.tw.
- 31. pre-PT.tw.
- 32. 25 or 26 or 27 or 28 or 29 or 30 or 31
- 33. 11 and 32
- 34. 24 or 33
- 35. remove duplicates from 34
- 36. cell transplant*.tw
- 37. bone marrow transplant*.tw.
- 38. 36 or 37
- 39. exp Organ Transplantation/
- 40. ((organ or heart or heart-lung or kidney or renal or liver or lung or pancreas) adj2 transplant*).tw.
- 41. 39 or 40
- 42. 38 and 41

- 43. 38 not 42
- 44. 35 not 43
- 45. animals/ not (humans/ and animals/)
- 46. 44 not 45
- 47. limit 46 to (editorial or letter)
- 48. 46 not 47
- 49. limit 48 to ed=20140201-20150228

EBM Review search strategy

- 1. exp Neoplasms/
- 2. neoplas*.tw.
- 3. cancer*.tw.
- 4. (tumour* or tumor*).tw.
- 5. malignan*.tw.
- 6. (oncology or oncologic or oncologist*).tw.
- 7. metasta*.tw.
- 8. carcinoma*.tw.
- 9. adenocarcinoma*.tw.
- 10. melanoma*.tw.
- 11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
- 12. Organ Transplantation/
- 13. exp Heart Transplantation/
- 14. Kidney Transplantation/
- 15. Liver Transplantation/
- 16. exp Lung Transplantation/
- 17. Pancreas Transplantation/
- 18. ((organ or heart or heart-lung or kidney or renal or liver or lung or pancreas) adj2 transplant*).tw.
- 19. 12 or 13 or 14 or 15 or 16 or 17 or 18
- 20. ((preexisting or pre-existing) adj5 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 21. (antecedent adj6 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 22. (history adj6 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 23. 20 or 21 or 22
- 24. 19 and 23
- 25. pretransplant*.tw.
- 26. pre-transplant*.tw.
- 27. (prior adj5 transplant*).tw.
- 28. pre-HT.tw.
- 29. pre-KT.tw.
- 30. pre-LT.tw.
- 31. pre-PT.tw.
- 32. 25 or 26 or 27 or 28 or 29 or 30 or 31
- 33. 11 and 32
- 34. 24 or 33
- 35. remove duplicates from 34
- 36. cell transplant*.tw.
- 37. bone marrow transplant*.tw.

- 38. 36 or 37
- 39. exp Organ Transplantation/
- 40. ((organ or heart or heart-lung or kidney or renal or liver or lung or pancreas) adj2 transplant*).tw.
- 41. 39 or 40
- 42. 38 and 41
- 43. 38 not 42
- 44. 35 not 43
- 45. limit 44 to yr="2014 -Current"

EMBASE Classic search strategy

- 1. exp neoplasm/
- 2. neoplas*.tw.
- 3. cancer*.tw.
- 4. (tumour* or tumor*).tw.
- 5. malignan*.tw.
- 6. (oncology or oncologic or oncologist*).tw.
- 7. metasta*.tw.
- 8. carcinoma*.tw.
- 9. adenocarcinoma*.tw.
- 10. melanoma*.tw.
- 11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
- 12. organ transplantation/
- 13. exp heart transplantation/
- 14. exp kidney transplantation/
- 15. exp liver transplantation/
- 16. exp lung transplantation/
- 17. exp pancreas transplantation/
- 18. ((organ or heart or heart-lung or kidney or renal or liver or lung or pancreas) adj2 transplant*).tw.
- 19. 12 or 13 or 14 or 15 or 16 or 17 or 18
- 20. ((preexisting or pre-existing) adj5 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 21. (antecedent adj6 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 22. (history adj6 (neoplas* or cancer* or tumour* or tumor* or malignan* or metasta* or carcinoma* or adenocarcinoma* or melanoma*)).tw.
- 23. 20 or 21 or 22
- 24. 19 and 23
- 25. pretransplant*.tw.
- 26. pre-transplant*.tw.
- 27. (prior adj5 transplant*).tw.
- 28. pre-HT.tw.
- 29. pre-KT.tw.
- 30. pre-LT.tw.
- 31. pre-PT.tw.
- 32. 25 or 26 or 27 or 28 or 29 or 30 or 31
- 33. 11 and 32
- 34. cell transplant*.tw.
- 35. bone marrow transplant*.tw.

- 36. 34 or 35
- 37. exp organ transplantation/
- 38. ((organ or heart or heart-lung or kidney or renal or liver or lung or pancreas) adj2 transplant*).tw.
- 39. 37 or 38
- 40. 36 and 39
- 41. 36 not 40
- 42. 33 not 41
- 43. animals/ not (humans/ and animals/)
- 44. 42 not 43
- 45. limit 44 to (editorial or letter)
- 46. 44 not 45
- 47. limit 46 to embase
- 48. limit 47 to dd=20140201-20150228

Appendix 2. List of sources included in the grey literature search

- 1. American Association for the Study of Liver Diseases
- 2. Israel Penn International Tumor Transplant Registry
- 3. Kidney Liver Foundation
- 4. National Kidney Foundation
- 5. Australian and New Zealand Dialysis and Transplant Registry
- 6. United Network for Organ Sharing
- 7. The International Society for Heart and Lung Transplantation
- 8. Transplant Cancer Match Study
- 9. Google Scholar

Appendix 3. Modified New-Castle Ottawa Coding Manual for Cohort Studies

Domain 1. Selection

- 1) Representativeness of the exposed cohort
 - a) Truly representative of the exposed individuals in the community *
 - b) Somewhat representative of the exposed individuals in the community \star
 - c) Selected group of users e.g. nurses, volunteers
 - d) No description of the derivation of the cohort
- 2) Selection of the non-exposed cohort
 - a) Drawn from the same community as the exposed cohort *
 - b) Drawn from a different source
 - c) No description of the derivation of the non-exposed cohort
- 3) Ascertainment of exposure
 - a) Secure record (e.g. surgical records) *
 - b) Record-linkage (e.g. cancer registry) *
 - c) Written self-report
 - d) No description

Domain 2. Comparability

- 1) Comparability of cohorts on the basis of the design or analysis
 - a) Study controls for recipient age and sex *
 - b) Study controls for any additional factor other than recipient age and sex *

Domain 3. Outcome

- 1) Assessment of outcome
 - a) Independent blind assessment *
 - b) Record linkage *
 - c) Self-report
 - d) No description
- 2) Was follow-up long enough for outcomes to occur
 - a) Yes (≥ 2 years)*
 - b) No
- 3) Adequacy of follow up of cohorts
 - a) Complete follow up all subjects accounted for *
 - b) Subjects lost to follow up unlikely to introduce bias small number lost > 10% follow up, or description provided of those lost \star
 - c) Follow up rate < 10% and no description of those lost
 - d) No statement

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability