Treatment and outcomes of unresectable and metastatic pancreatic cancer treated in public and private Australian hospitals

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Abstract *(Word count: 250)*

Background: Prior studies have reported for several cancer types that treatment in the private sector is associated with improved survival outcomes. Data for patients with locally advanced unresectable and metastatic pancreatic ductal adenocarcinoma (PDAC) has not previously been reported.

Methods: Analysis of patients from January 2016 to June 2020 registered to a multi-centre prospective cancer database. Baseline demographic and clinicopathologic characteristics were compared. The Kaplan-Meier method was used to compare overall survival (OS). Multivariate Cox and logistic regression analyses were used to determine predictors of mortality and first-line chemotherapy treatment, respectively.

Results: Of 822 patients, 22.5% received private care. Private patients were older (median 71.5 years vs. 68.9 years, p = <0.05), had better performance status (ECOG 0 to 1: 82.2% vs. 73.5%, p = 0.05) and more likely to reside in an area with high socio-economic advantage (67.0% vs. 19.6%, p = <0.01). Private patients were more likely to receive first-line chemotherapy (69.7% vs. 54.2%, p = <0.01) with logistic regression demonstrating private care (OR 1.87, 95% CI 1.20 to 2.97) as an independent predictor of receiving chemotherapy. Private patients had prolonged survival (median OS 9.2 vs. 6.9 months, HR 1.2, p = 0.05). Receiving first-line chemotherapy was an independent predictor of mortality, but private care was not.

Conclusion: Care in the private system is associated with improved overall survival, with higher uptake of first-line chemotherapy appearing to be the main contributor. Given the discrepancy, further studies are needed to determine what factors are driving this difference.

Keypoints:

- Treatment of metastatic and locally unresectable pancreatic cancer in the private health sector is associated with improved median overall survival compared to the public sector.
- Treatment in the private sector is an independent predictor of receiving first-line chemotherapy even after adjusting for baseline demographic variables.

Declarations

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Introduction

Pancreatic cancer is the eight most commonly diagnosed cancer in Australia but the 3rd leading cause of cancer-related death[1]. Despite advances in cancer diagnosis and care, the 5-year survival from pancreatic ductal adenocarcinoma (PDAC) is still less than 10% [2]. For the 40% of patients diagnosed with distant metastases, the 5-year survival rate is less than 3% [2].

Medicare has been Australia's universal healthcare scheme since 1984 [3]. Through general revenue and taxpayer funds, this national government program provides Australian citizens with equitable access to healthcare services. For Australian cancer patients treated in public government-run hospitals, the Medicare scheme ensures access to oncology specialists, chemotherapy delivery, surgery and other cancer-related care at little or no out-of-pocket costs. However, patients may also additionally purchase private health insurance and elect to receive treatment through the private health sector, which may afford benefits such as reduced waiting times and treatment by your physician of choice. However, costs are borne by patients directly or through their insurance provider. Prior Australian and international retrospective studies have observed superior survival outcomes for patients treated in private hospitals compared to public across a number of cancer types such as colorectal, breast and lung [4 – 8]. Reasons for this disparity has continued to be explored but likely encompasses patient and sociodemographic factors as well as clinician and institutional considerations. This survival disparity has not been evaluated in patients with pancreatic cancer.

Utilising data from a multi-centre prospectively maintained pancreatic cancer registry, we aim to compare patients with locally advanced unresectable or metastatic PDAC treated in Australian public versus private health sector. Additionally, we take into account

demographic, clinicopathological and treatment factors to discuss potential reasons for any observed differences.

Methods

Data collection

This study utilised data from patients registered to the Pancreatic Cancer: Understanding Routine Practice and Lift Ending Results (PURPLE) registry (ACTRN1261700147437) [9]. The PURPLE registry is an ethically approved prospective database cataloguing patients diagnosed with pancreatic cancer from 32 cancer centres across Australasia. This international pancreatic cancer registry enables the collection of comprehensive data across a spectrum of metropolitan, regional, public and private care systems. All stages of pancreatic are captured, with the entire treatment journey prospectively tracked from diagnosis.

All patients with locally advanced unresectable or metastatic pancreatic ductal adenocarcinoma (PDAC), as assessed by the treating physician according to the National Comprehensive Cancer Network resectability guidelines, diagnosed at participating Australian sites from registry registration (January 2016) to June 2020 were included in this analysis [10]. Patients with resectable or borderline resectable cancers were excluded. Additionally any patients initially deemed to have locally advanced unresectable who were subsequently resected were also excluded.

Study design and variables of interest

The study used a retrospective cohort design. Patients were stratified according to sector of care (private versus public). Baseline demographics were selected based on their likelihood to impact treatment decision making and outcomes, including: age, gender, Eastern Co-Operative Group

performance status (ECOG) and Charlson Comorbidity Index (CCI). Estimates of socio-economic status were assessed based on a patient's residential address based on the Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD) [11]. The IRSAD score arranges Australian postcodes by quintile, with a low score indicating greater disadvantage and a high score indicating a greater advantage.

Clinicopathological data included the presence of symptoms at diagnosis, the anatomical location of the pancreatic tumour and stage (locally advanced unresectable vs. metastatic). Treatment data included the initial type of treatment and receipt of chemotherapy 30 days prior to death.

Outcome

The primary outcome measure was overall survival (OS), calculated in months as time from diagnosis of pancreatic cancer to death from any cause. Patients alive at time of data extraction were censored at the date of last medical review.

Statistical analysis

Patient demographics and clinicopathological data were described as frequencies and percentages for binary and categorical variables. Age was also described with means and standard deviation. Differences in characteristics between patients treated in the public and private sector were examined with the Chi squared test. The characteristics of patients who received chemotherapy as their first-line treatment were also compared with differences examined with the Chi squared test. The association between receipt of chemotherapy and patient characteristics including treatment in the private or public sector was further evaluated with binomial logistic regression providing odds ratios and 95% confidence interval for each co-variate. The Kaplan-Meier method was used to compare OS. A Cox proportional hazards model was used to assess if treatment in private or public sector influenced median OS. Two-sided p-values <0.05 were considered statistically significant. All analyses were performed using R statistical software, version 3.6.3.

Results

Patient demographics

Of 822 patients with locally advanced unresectable and metastatic PDAC, 185 (22.5%) were treated in the private sector and 637 (77.5%) were treated in the public sector. Table 1 presents the characteristics of private and public patients. Private patients were significantly older (median 71.5 years vs. 69.0 years, p = <0.01), had better EOCG (0 to 1: 82.2% vs. 73.5%, 2+: 17.3 vs. 25.7%, p = 0.05) and more likely to reside in a higher IRSAD quintile (IRSAD 5: 67.0% vs. 19.6%, p = <0.01).

Clinicopathological characteristics

There was no difference in the proportion of patients with locally advanced unresectable or metastatic disease (private vs. public; locally advanced 33.5% vs. 36.9%, metastatic 66.5% vs. 63.1%, p = 0.45).

Treatment characteristics

Public patients were more likely to receive best supportive care only (40.0% vs. 25.4%, p = <0.001). Chemotherapy was the most common first-line treatment and private patients were more likely to receive this modality (69.7% vs. 54.2%, p = <0.01).

Patients receiving first-line chemotherapy

Table 2 presents the demographic and treatment characteristics in patients receiving first-line chemotherapy. Private patients who received chemotherapy were older than public patients (median 69.2 years vs. 65.6 years, p <0.01) but there was no significant difference in gender, ECOG or CCI. Treated private patients were likely to reside in a higher IRSAD quintile (IRSAD 5: 67.4% vs. 22.6%, p <0.01). The most common first-line chemotherapy regimens were single agent gemcitabine (private vs. public: 7.6% vs. 14.2%, p = 0.06) and combination gemcitabine/nab-paclitaxel (81.7% vs. 65.2%, p <0.05) with only relatively small proportion of patients receiving triplet FOLFIRINOX (6.2% vs 13.6%, p = 0.03). Private patients received more means lines of therapy (1.75 lines vs. 1.43 lines, p = <0.01) and were more likely to receive 3 or more lines of therapy (22.5% vs. 8.7%, p < 0.001). Private patients were also more likely to receive chemotherapy in the 30 days prior to death (13.2% vs. 6.7%, p = 0.04).

Results from the logistic regression are presented in Supplementary Table 1. The logistic regression demonstrated being <70 years (OR 2.71, 95% CI 1.95 to 3.86), being treated in the private sector (OR 1.89, 95% CI 1.22 to 2.97) and having an ECOG of 0 to 1 (OR 3.20, 95% CI 2.21 to 4.67) were independent predictors of receiving first-line chemotherapy.

Survival

In the overall population, median OS (mOS) was increased in patients treated in the private sector (9.2 vs. 6.9 months; HR 1.2, 95% CI 1.02 to 1.48, p = 0.05, Figure 1). Patients who received first-line chemotherapy were associated with improved median OS but survival was similar between private and public sector (9.9 vs. 9.1 months; HR 1.1, 95% CI 0.88 to 1.39, p = 0.5, Figure 2). Improved median OS was observed for public patients residing in IRSAD quintile 5 compared to less socioeconomic advantageous quintiles (8.3 vs. 6.6 months; HR 0.78, 95% CI 0.62 to 0.97, p = 0.02) but not private (9.4 vs. 6.8 months, HR 0.98, 95% CI 0.66 to 1.48, p = 0.9, Figure 3).

Results from the multivariate Cox regression analysis are presented in the supplementary material. Age category (<70 vs. ≥ 70 years), being treated in private vs. public sector, ECOG, CCI, IRSAD score, stage of cancer (locally advanced vs. metastatic) and receipt of first-line chemotherapy were selected as co-variates. The analysis demonstrated that having an ECOG of 0 to 1 (OR 0.53, 95% CI 0.44 to 0.65), being locally advanced (OR 0.50, 95% CI 0.42 to 0.59) and receiving first-line chemotherapy (OR 0.49, 95% CI 0.40 to 0.58) reduced the risk of death.

Discussion

To our knowledge, this study presents the first comparison of outcomes in private versus public patients diagnosed with locally advanced unresectable or metastatic PDAC. Our major finding is that

patients in the private sector were more likely to receive chemotherapy, and that this translated into a modest survival advantage. Our median survival for patients electing supportive treatment only and for patients receiving chemotherapy were in line with multiple other reported series, demonstrating a modest benefit for the use of chemotherapy, but without any long term or exceptional responders [12 - 16]. This modest benefit must therefore be balanced against the side-effects of treatment.

Prior Australian and international retrospective studies have also observed superior survival outcomes for patients treated in private hospitals compared to public hospitals across a range of other cancers including colorectal, breast and lung [4- 8]. Multi-variate analyses carried out by these studies have consistently identified being treated in the private sector as an independent predictor of reduced mortality even after adjusting for baseline demographic variables [4, 5, 8]. Suggested reasons for this difference have included the potential undertreatment of public patients amongst other factors. Undertreatment many include fewer patients proceeding to surgery, being less likely to receive chemotherapy or being less likely to receive combination chemotherapy including the use of biologics [4, 5, 8]. In our study, even after adjusting for age, functional status and co-morbidities, treatment in the private sector was an independent predictor of receiving first-line chemotherapy. It is unclear whether this is due to patient factors or clinician preference but we consider potential reasons in later discussion.

We also noted that patients receiving chemotherapy were treated more intensively in the private sector (more lines of chemotherapy, more likely to receive chemotherapy in the 30 days prior to their death) yet this more aggressive approach did not result in any significant survival benefit compared to public patients who received less lines of chemotherapy. Whilst there is limited evidence from randomised trials to support subsequent lines of chemotherapy following progression, the reported survival benefits are modest and optimal treatment post-FOLFIRINOX is unknown [17 – 20]. This suggests that most of the chemotherapy benefit from treatment occurs in first line, and better patient selection for subsequent treatment and novel approaches are needed. Notably, only 1.1% of patients in either sector were treated on clinical trials.

The noted differences in treatment patterns between private and public patients could have multiple drivers. These factors, broadly categorised as patient, clinician and institutional, will be discussed in turn.

Patient factors

The higher proportion of private patients residing in an IRSAD quintile of 5 likely reflects socioeconomic disparities between the patient populations. Although our study is the first to directly compare private to public patients, previous studies primarily conducted in the United States have noted disparities in pancreatic cancer outcomes based on socio-demographic factors such as ethnicity, insurance status and socioeconomic factors [21 – 26]. Patients with lower socio-economic status were more likely to present with later staged disease, less likely to receive treatment such as surgery or chemotherapy and ultimately, have poorer reported survival outcomes. Possessing private insurance is therefore likely reflective of a higher socio-economic status and this in turn influences treatment decision making and outcomes. Reasons for this discrepancy could be different levels of health literacy, issues with health care access, and differing experiences of financial toxicity as a result of cancer diagnosis and treatment. Lower socio-economic status is also associated with mortality risk factors such as smoking, alcohol use and cardiovascular comorbidities, although co-morbidities as measured by CCI were well matched in our study [27]. Although our study demonstrated that residency in areas with greatest socioeconomic advantage was associated with improved survival amongst public patients but not private, IRSAD quintile was not independently associated with receipt of chemotherapy or mortality, suggesting that socioeconomic status alone does not explain the differences. In regards to the issue of potential overtreatment, it is conceivable that private patients have different health seeking behaviour and the financial capacity and level of social support to pursue multiple lines of therapy.

Clinician factors

As clinicians in the private sector are renumerated for patients receiving treatment, there is a conceivable financial incentive for a clinician to recommend intravenous treatment. Previous data

from patients with metastatic colorectal cancer also does not support an undue impact of financial incentives on care delivered [4]. In our study, a significantly lower proportion of private patients received FOLFIRINOX, reflecting a hesitancy to expose an older and feasibly more frail population to triplet chemotherapy, although ECOG and co-morbidities index were well matched to public patients. Reduced FOLIFIRNOX uptake may also explain why private patients received more lines of therapy as although evidence supports the use of subsequent fluorouracil-based chemotherapy following gemcitabine-containing treatment, the optimal treatment following FOLFIRINOX is unknown[10]. However, the lack of survival benefit and the higher proportion of patients receiving chemotherapy in the 30 days prior to death highlights the need for careful consideration of treatment futility in subsequent lines.

Institutional factors

Differences may exist between public and private institutions in regards to time from referral to first oncologist review, delays in accessing imaging and access to other specialists as well as time to initiating therapy. The PURPLE registry does not measure such metrics so we cannot present any data that directly demonstrates any deficits. Given the body of work that consistently reports survival difference between private and public patients, questions of access to and issues with navigation of the healthcare system are important areas of research.

There are several limitations of this study. First, this is a retrospective study and so the possibility of unmeasured confounding factors existing between private and public patients needs to be acknowledged. We have adjusted for identified confounding factors such as age, performance status, CCI and IRSAD score in our logistic regression and multivariate Cox regression analysis. Second, the majority of patients came from large metropolitan centres. This may influence the results as there is known discrepancy in outcomes between metropolitan and regional sites. Third, resectability was determined and recorded in the PURPLE registry by the treating physician. Whether the patients were discussed in multi-disciplinary meetings is unknown however, we excluded patients that received neoadjuvant treatment or had successful resection so the likelihood of including potentially resectable patients is low. Fourth, some patients may have transitioned between private and public care, resulting in misclassification. Possible reasons for this could be access to trials or patient choice. Finally,

despite utilising data from a prospectively maintained database, there was still missing data. Most significantly was the significant number of private patients whose referral to palliative care status was unknown. We excluded this as a variable in our analysis.

Conclusion

We report on the first comparison of survival outcomes between patients with locally advanced unresectable and metastatic pancreatic cancer treated in the private and public sector based on data from a multi-centre prospectively maintained database. Private patients had improved survival driven principally by the higher uptake of chemotherapy treatment in comparison to public patients. Given that first-line chemotherapy treatment is associated with improved survival in unresectable and metastatic pancreatic cancer, further efforts should be made to explore and improve chemotherapy treatment uptake amongst public patients.

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Figure 1 Overall survival, Kaplan-Meier comparison between private and public patients.

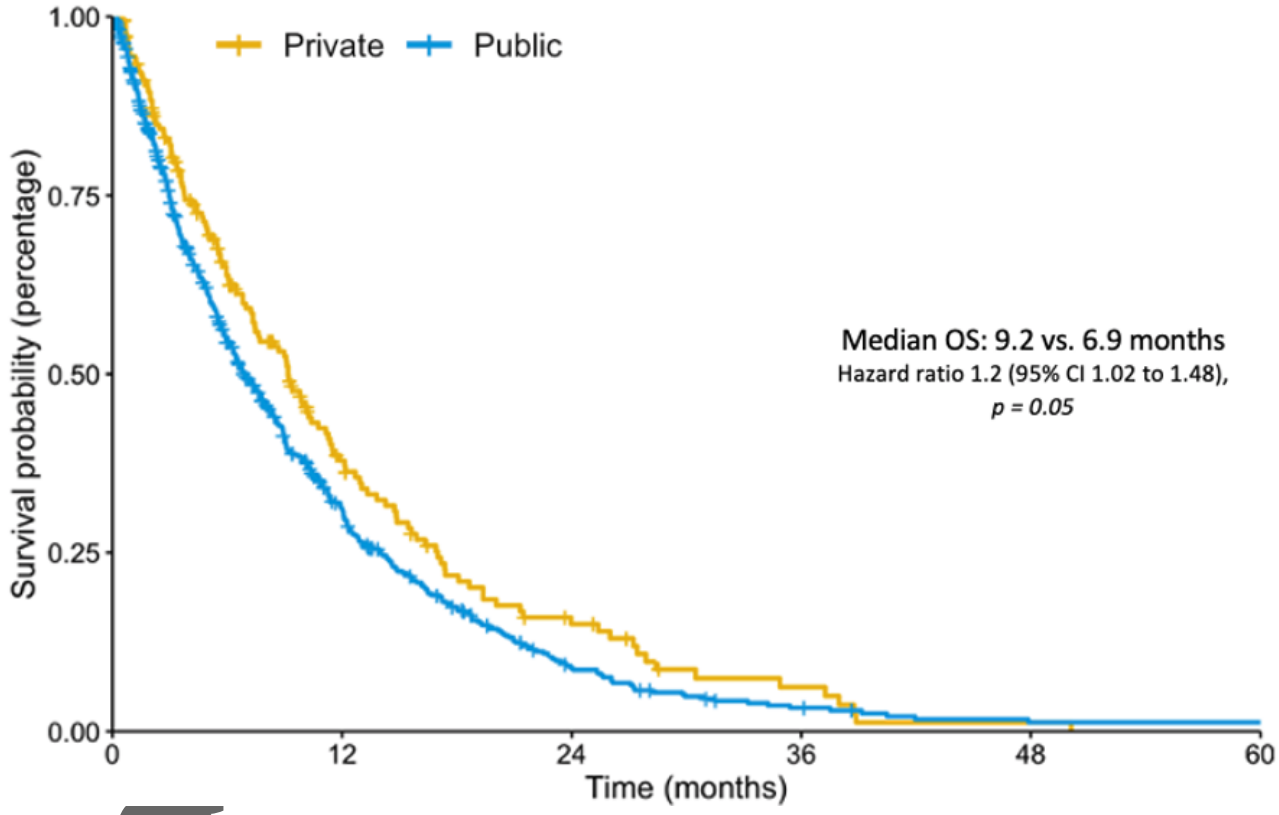

Figure 2 Overall survival, Kaplan-Meier comparison between private and public patients who received first-line chemotherapy

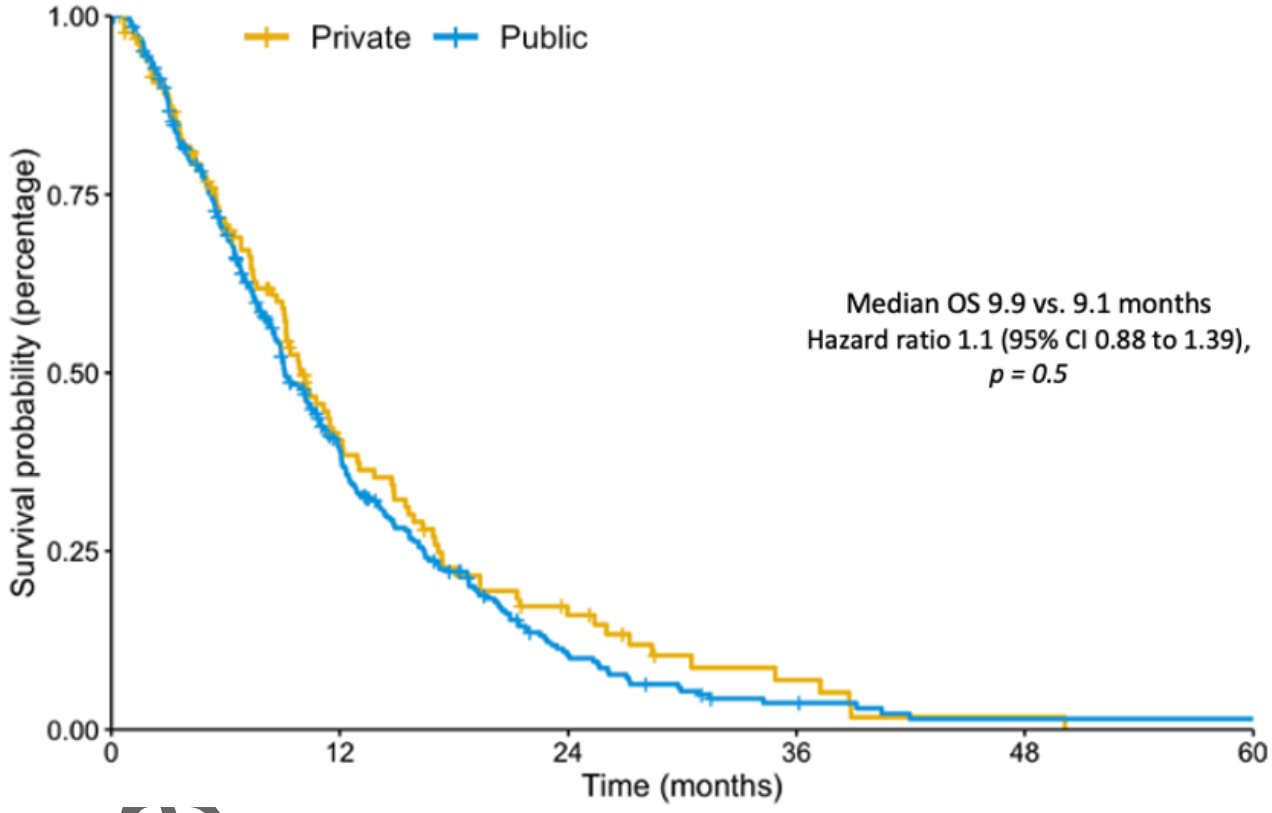

Figure 3. Overall survival, stratified by Index of Socio-economic advantage and disadvantage (IRSAD) and sector of care

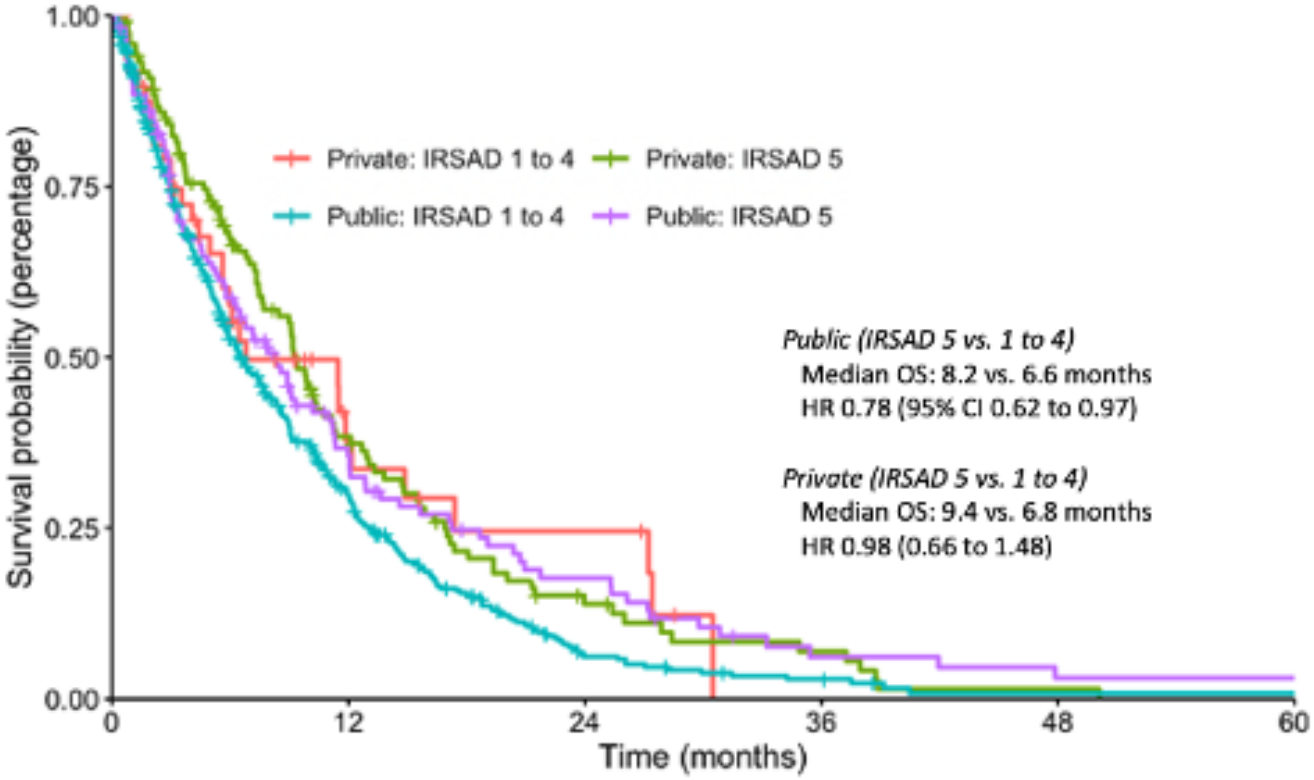

Table 1 Patient demographics, clinicopathological and treatment characteristics

	Private (n = 185)	Public (n = 637)	p-test

Age (mean (SD))	71.5 (10.8)	68.9 (11.6)	<0.01
Gender (%)			0.76
M	94 (50.8)	323 (50.7)	
F	91 (49.2)	311 (48.8)	
Missing data	0 (0.0)	3 (0.5)	
ECOG (%)			0.05
0 to 1	152 (82.2)	468 (73.5)	
2+	32 (17.3)	164 (25.7)	
Missing data	1 (0.5)	5 (0.8)	
Charlson co-morbidity index (%)			0.253
0 to 1	22 (11.8)	86 (13.5)	
2 to 4	118 (63.1)	351 (55.0)	
5 to 7	40 (21.4)	161 (25.2)	
8 to 10	4 (2.1)	32 (5.0)	
>10	2 (1.1)	3 (0.5)	
Missing data	1 (0.5)	5 (0.8)	
IRSAD quintile (%)			<0.01
1 to 4	50 (27.0)	467 (73.3)	
5 (greatest advantage)	124 (67.0)	125 (19.6)	
Missing data	11 (5.9)	45 (7.1)	
Symptoms at diagnosis (%)	158 (85.4)	569 (89.3)	0.26
Stage (%)			0.45
Local	62 (33.5)	235 (36.9)	
Metastatic	123 (66.5)	402 (63.1)	
Primary tumour site (%)			<0.01

Head	79 (42.7)	370 (58.1)	
Body	42 (22.7)	114 (17.9)	
Tail	35 (18.9)	119 (18.7)	
Whole organ	3 (1.6)	4 (0.6)	
Missing data	26 (14.1)	30 (4.7)	
Received best supportive care only (%)	47 (25.4)	259 (40.0)	< 0.01
Initial treatment (%)			
Chemotherapy	129 (69.7)	345 (54.2)	
Chemoradiation	3 (1.6)	10 (1.6)	
Palliative surgery	0 (0.0)	6 (0.9)	
Radiotherapy	3 (1.6)	1 (0.2)	
Trial	2 (1.1)	7 (1.1)	
Data missing	1 (0.5)	9 (1.4)	

Table 2 Demographic and treatment characteristics in patients receiving first line chemotherapy

Stratified by Public/Private - Chemotherapy			
	Private (n = 129)	Public (n = 345)	p-value
Age (mean (SD))	69.07 (9.7)	65.58 (10.1)	<0.01
Gender (%)			0.39
M	61 (47.3)	181 (52.5)	
F	68 (52.7)	162 (47.0)	
Missing data	0 (0.0)	2 (0.6)	

ECOG (%)			0.07
0 - 1	118 (91.5)	288 (83.5)	
2+	11 (8.5)	53 (15.4)	
Missing data	0	4 (1.2)	
Charlson co-morbidity index(%)			0.557
0 - 1	18 (13.7)	56 (16.8)	
2 to 4	93 (7.1)	219 (63.5)	
5 to 7	17 (13.0)	52 (15.1)	
8 to 10	2 (1.5)	10 (2.9)	
>10	1 (0.8)	2 (0.6)	
Missing data	0 (0.0)	4 (1.2)	
IRSAD quintile (%)			<0.01
1 to 4	35 (27.1)	248 (71.9)	
5 (greatest advantage)	87 (67.4)	78 (22.6)	
Missing data	7 (5.4)	19 (5.5)	
Stage (%)			0.40
Local unresectable	40 (31.0)	117 (33.9)	
Metastatic	89 (69.0)	228 (66.1)	
First-line chemotherapy regimen			
Single	10 (7.8)	52 (15.1)	<0.01
Doublet	108 (83.7)	235 (68.1)	
Triplet	8 (6.2)	47 (13.6)	
Missing data	3 (2.3)	11 (3.2)	
Mean no. of lines (mean SD)	1.75 (1.1)	1.43 (0.7)	<0.01
No. of lines (%)			<0.01

1 to 2	100 (77.5)	315 (91.3)	
3+	29 (22.5)	30 (8.7)	
Chemotherapy less than 30 days prior to death (%)	17 (13.2)	23 (6.7)	0.04

Predictor	Univariable analysis OR (95% CI)	Multivariable analysis OR (95% CI)
Age ≤ 70 years	2.87 (2.14 to 3.87)	2.71 (1.91 to 3.86)
Treatment in private sector	2.10 (1.48 to 3.03)	1.89 (1.22 to 2.97)
ECOG 0 to 1	4.23 (3.08 to 6.11)	3.20 (2.21 to 4.67)
Charlson Comorbidity Index 0 to 1	2.28 (1.46 to 3.71)	1.25 (0.73 to 2.19)
Index of Relative Socioeconomic Advantage and Advantage of 5 (most advantageous)	1.69 (1.23 to 2.34)	1.39 (0.95 to 2.05)
Locally unresectable primary	0.73 (0.55 to 0.87)	0.72 (0.52 to 1.00)
Intercept = 0.37; representing a patient with: age over 70 years, treated in the public sector, ECOG 2+, Charlson Comorbidity Index 2+, presiding in IRSAD 1 to 4 quintile and diagnosed with distant metastases		

Predictor	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)
Age ≤ 70 years	0.69 (0.59 to 0.80)	0.86 (0.71 to 1.03)
Treatment in private sector	0.81 (0.67 to 0.98)	1.00 (0.80 to 1.25)
ECOG (0 to 1)	0.46 (0.38 to 0.55)	0.53 (0.44 to 0.65)

Charlson Comorbidity Index (0 to 1)	0.73 (0.58 to 0.92)	0.92 (0.71 to 1.19)
Index of Relative Socioeconomic Advantage and Advantage of 5 (most advantageous)	0.78 (0.66 to 0.93)	0.84 (0.69 to 1.02)
Locally unresectable primary	0.58 (0.49 to 0.69)	0.50 (0.42 to 0.59)
Received first line chemotherapy	0.49 (0.42 to 0.58)	0.48 (0.40 to 0.58)

	Private (n = 185)	Public (n = 637)	p-test
Age (mean (SD))	71.5 (10.8)	68.9 (11.6)	<0.01
Gender (%)			0.76
M	94 (50.8)	323 (50.7)	
F	91 (49.2)	311 (48.8)	
Missing data	0 (0.0)	3 (0.5)	
ECOG (%)			0.05
0 to 1	152 (82.2)	468 (73.5)	
2+	32 (17.3)	164 (25.7)	
Missing data	1 (0.5)	5 (0.8)	
Charlson co-morbidity index (%)			0.253
0 to 1	22 (11.8)	86 (13.5)	
2 to 4	118 (63.1)	351 (55.0)	
5 to 7	40 (21.4)	161 (25.2)	
8 to 10	4 (2.1)	32 (5.0)	
>10	2 (1.1)	3 (0.5)	
Missing data	1 (0.5)	5 (0.8)	

IRSAD quintile (%)			<0.01
1 to 4	50 (27.0)	467 (73.3)	
5 (greatest advantage)	124 (67.0)	125 (19.6)	
Missing data	11 (5.9)	45 (7.1)	
Symptoms at diagnosis (%)	158 (85.4)	569 (89.3)	0.26
Stage (%)			0.45
Local	62 (33.5)	235 (36.9)	
Metastatic	123 (66.5)	402 (63.1)	
Primary tumour site (%)			<0.01
Head	79 (42.7)	370 (58.1)	
Body	42 (22.7)	114 (17.9)	
Tail	35 (18.9)	119 (18.7)	
Whole organ	3 (1.6)	4 (0.6)	
Missing data	26 (14.1)	30 (4.7)	
Received best supportive care only (%)	47 (25.4)	259 (40.0)	< 0.01
Initial treatment (%)			
Chemotherapy	129 (69.7)	345 (54.2)	
Chemoradiation	3 (1.6)	10 (1.6)	
Palliative surgery	0 (0.0)	6 (0.9)	
Radiotherapy	3 (1.6)	1 (0.2)	
Trial	2 (1.1)	7 (1.1)	
Data missing	1 (0.5)	9 (1.4)	

Stratified by Public/Private - Chemotherapy

	Private (n = 129)	Public (n = 345)	p-value
Age (mean (SD))	69.07 (9.7)	65.58 (10.1)	<0.01
Gender (%)			0.39
M	61 (47.3)	181 (52.5)	
F	68 (52.7)	162 (47.0)	
Missing data	0 (0.0)	2 (0.6)	
ECOG (%)			0.07
0 - 1	118 (91.5)	288 (83.5)	
2+	11 (8.5)	53 (15.4)	
Missing data	0	4 (1.2)	
Charlson co-morbidity index(%)			0.557
0 - 1	18 (13.7)	56 (16.8)	
2 to 4	93 (7.1)	219 (63.5)	
5 to 7	17 (13.0)	52 (15.1)	
8 to 10	2 (1.5)	10 (2.9)	
>10	1 (0.8)	2 (0.6)	
Missing data	0 (0.0)	4 (1.2)	
IRSAD quintile (%)			<0.01
1 to 4	35 (27.1)	248 (71.9)	
5 (greatest advantage)	87 (67.4)	78 (22.6)	
Missing data	7 (5.4)	19 (5.5)	
Stage (%)			0.40
Local unresectable	40 (31.0)	117 (33.9)	
Metastatic	89 (69.0)	228 (66.1)	

First-line chemotherapy regimen			
Single	10 (7.8)	52 (15.1)	<0.01
Doublet	108 (83.7)	235 (68.1)	
Triplet	8 (6.2)	47 (13.6)	
Missing data	3 (2.3)	11 (3.2)	
Mean no. of lines (mean SD)	1.75 (1.1)	1.43 (0.7)	<0.01
No. of lines (%)			<0.01
1 to 2	100 (77.5)	315 (91.3)	
3+	29 (22.5)	30 (8.7)	
Chemotherapy less than 30 days prior to death (%)	17 (13.2)	23 (6.7)	0.04