SOCIAL DEPRIVATION AND PROGNOSIS IN SCOTTISH PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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ONLINE DATA SUPPLEMENT

Multivariate Analysis

Cox multivariate regression analysis was performed to adjust for other independent predictors of mortality to ensure that this did not result in a significant association between social deprivation and mortality. Variables were included in the analysis if they were significantly associated with mortality on univariate analysis or showed a significant relationship with deprivation quintile. As several of the variables had significant numbers of missing values (especially 6MWD, TLco, NTproBNP and CAMPHOR score), inclusion of all in one model would impair the efficacy of the analysis. Instead, five multivariate models were constructed, each containing a core set of variables where few variables were missing (time since diagnosis, age, sex, BMI, RAP, CO and SvO_2) and only one of 6MWD, TLco, NTproBNP

and CAMPHOR score (three elements analysed). No significant association between social deprivation and all-cause mortality was present in any of these models. Results of the analyses are shown in Tables S1 to S6 below.

Table S1. Multivariate analysis of prediction of all-cause mortality by baseline variables including core variables and 6MWD (Model 1). (N=174)

	HR	**95% Confidence Interval**	**p-value**
Diagnosis year	1.01	(0.93 – 1.11)	0.74
Age years	1.04	(1.02 - 1.07)	**<0.001**
Sex (Male)	2.01	(1.18 – 3.41)	**0.010**
BMI kg/m^2	1.00	(0.95 – 1.05)	1.00
RAP mm Hg	1.04	(0.98 – 1.09)	0.17
CO L/min	1.02	(0.78 – 1.35)	0.86
SvO_2 %	1.00	(0.97 – 1.04)	1.00
6MWD m	0.998	(0.995 – 1.00)	**0.050**
Deprivation Quintile 1	1.23	(0.63 – 2.42)	0.54
Deprivation Quintile 2	1.03	(0.51 – 2.09)	0.93
Deprivation Quintile 3	1.09	(0.46 – 2.56)	0.85
Deprivation Quintile 4	0.74	(0.32 – 1.69)	0.48
Deprivation Quintile 5 (ref)	1.0		

N – number, HR – hazard ratio, BMI – body mass index, RAP – right atrial pressure, CO – cardiac output, SvO_2 – mixed venous oxygen saturation, 6MWD – six minute walk distance.

Table S2. Multivariate analysis of prediction of all-cause mortality by baseline variables including core variables and Log_{10}NTproBNP (Model 2). (N=171)

	HR	**95% Confidence Interval**	**p-value**
Diagnosis year	0.92	(0.84 - 1.01)	0.093
Age years	1.05	(1.03 - 1.07)	**<0.001**
Sex (Male)	1.73	(1.07 – 2.82)	**0.026**
BMI kg/m^2	1.03	(0.98 – 1.07)	0.24
RAP mm Hg	1.00	(0.95 – 1.06)	0.87

CO L/min	0.93	(0.69 – 1.24)	0.60
SvO_2 %	0.99	(0.96 – 1.03)	0.72
Log_{10}NTproBNP	2.11	(1.26 – 3.55)	**0.005**
Deprivation Quintile 1	1.43	(0.73 – 2.79)	0.30
Deprivation Quintile 2	1.08	(0.53 – 2.19)	0.83
Deprivation Quintile 3	1.30	(0.63 – 2.68)	0.48
Deprivation Quintile 4	0.85	(0.38 – 1.90)	0.69
Deprivation Quintile 5 (ref)	1.0		

N – number, HR – hazard ratio, BMI – body mass index, RAP – right atrial pressure, CO – cardiac output, SvO_2 – mixed venous oxygen saturation, 6MWD – six minute walk distance. NTproBNP – N-terminal pro-B type natriuretic peptide.

Table S3. Multivariate analysis of prediction of all-cause mortality by baseline variables including core variables and TLCO % pred (Model 3). (N=201)

	HR	**95% Confidence Interval**	**p-value**
Diagnosis year	0.99	(0.92 – 1.07)	0.76
Age years	1.03	(1.01 - 1.05)	**0.002**
Sex (Male)	1.49	(0.95 – 2.34)	0.086
BMI kg/m^2	1.00	(0.95 – 1.04)	0.91
RAP mm Hg	1.04	(0.99 – 1.09)	0.13
CO L/min	0.95	(0.73 – 1.23)	0.71
SvO_2 %	0.98	(0.95 – 1.00)	0.075
TLCO % pred	0.97	(0.96 – 0.98)	**<0.001**
Deprivation Quintile 1	0.97	(0.50 – 1.89)	0.93
Deprivation Quintile 2	0.78	(0.40 – 1.53)	0.48
Deprivation Quintile 3	1.04	(0.51 – 2.11)	0.92
Deprivation Quintile 4	0.68	(0.33 – 1.40)	0.30
Deprivation Quintile 5 (ref)	1.0		

N – number, HR – hazard ratio, BMI – body mass index, RAP – right atrial pressure, CO – cardiac output, SvO_2 – mixed venous oxygen saturation, TLCO – transfer factor.

Table S4. Multivariate analysis of prediction of all-cause mortality by baseline variables including core variables and CAMPHOR Composite Score (Model 4). (N=87)

	HR	95% Confidence Interval	p-value
Diagnosis year	0.92	(0.81 – 1.04)	0.20
Age years	1.05	(1.02 - 1.09)	**<0.001**
Sex (Male)	2.37	(1.12 – 5.00)	**0.023**
BMI kg/m^2	1.03	(0.98 – 1.09)	0.23
RAP mm Hg	1.02	(0.96 – 1.10)	0.50
CO L/min	0.81	(0.54 – 1.20)	0.29
SvO_2 %	0.98	(0.94 – 1.03)	0.50
CAMPHOR Composite Score	1.01	(0.99 – 1.04)	0.20
Deprivation Quintile 1	0.99	(0.33 – 2.94)	0.99
Deprivation Quintile 2	0.60	(0.20 – 1.82)	0.37
Deprivation Quintile 3	1.89	(0.67 – 5.41)	0.23
Deprivation Quintile 4	1.11	(0.37 – 3.35)	0.85
Deprivation Quintile 5 (ref)	1.0		

N – number, HR – hazard ratio, BMI – body mass index, RAP – right atrial pressure, CO – cardiac output, SvO_2 – mixed venous oxygen saturation, CAMPHOR - Cambridge Pulmonary Hypertension Outcome Review.

Table S5. Multivariate analysis of prediction of all-cause mortality by baseline variables including core variables and CAMPHOR Activities (Model 5). (N=87)

	HR	95% Confidence Interval	p-value
Diagnosis year	0.89	(0.78 – 1.01)	0.072
Age years	1.05	(1.02 - 1.08)	**0.003**
Sex (Male)	2.20	(1.03 – 4.67)	**0.041**
BMI kg/m^2	1.03	(0.97 – 1.09)	0.33
RAP mm Hg	1.02	(0.94 – 1.09)	0.66
CO L/min	0.82	(0.55 – 1.21)	0.31
SvO_2 %	0.98	(0.94 – 1.02)	0.36
CAMPHOR Activities	1.07	(1.01 – 1.14)	**0.014**
Deprivation Quintile 1	0.87	(0.29 – 2.58)	0.80
Deprivation Quintile 2	0.54	(0.18 – 1.64)	0.28
Deprivation Quintile 3	1.81	(0.63 – 5.14)	0.27
Deprivation Quintile 4	1.21	(0.40 – 3.69)	0.73
Deprivation Quintile 5 (ref)	1.0		

N – number, HR – hazard ratio, BMI – body mass index, RAP – right atrial pressure, CO – cardiac output, SvO_2 – mixed venous oxygen saturation, CAMPHOR - Cambridge Pulmonary Hypertension Outcome Review.

Table S6. Multivariate analysis of prediction of all-cause mortality by baseline variables including core variables and CAMPHOR QOL (Model 6). (N=87)

	HR	95% Confidence Interval	p-value
Diagnosis year	0.93	(0.82 – 1.05)	0.25
Age years	1.06	(1.03 - 1.09)	**<0.001**
Sex (Male)	2.35	(1.12 – 4.94)	**0.024**
BMI kg/m^2	1.04	(0.98 – 1.09)	0.19
RAP mm Hg	1.03	(0.96 – 1.10)	0.45
CO L/min	0.79	(0.54 – 1.17)	0.25
SvO_2 %	0.98	(0.94 – 1.03)	0.51
CAMPHOR QOL	1.02	(0.97 – 1.08)	0.36
Deprivation Quintile 1	1.04	(0.35 – 3.12)	0.94
Deprivation Quintile 2	0.63	(0.21 – 1.91)	0.41
Deprivation Quintile 3	1.96	(0.69 – 5.57)	0.20
Deprivation Quintile 4	1.09	(0.36 – 3.31)	0.88
Deprivation Quintile 5 (ref)	1.0		

N – number, HR – hazard ratio, BMI – body mass index, RAP – right atrial pressure, CO – cardiac output, SvO_2 – mixed venous oxygen saturation, CAMPHOR - Cambridge Pulmonary Hypertension Outcome Review, QOL – quality of life.

Analysis by Gender

Given the preponderance of male subjects in quintile 5, the analysis was repeated for the dataset divided by gender. The baseline characteristics for females divided by quintile are shown in Table S7 and for males in Table S8.

Table S7. Baseline characteristics for female subjects and across SIMD quintiles.

Variable	All Subjects	Deprivation Quintile					p-value*
		1- most deprived	2	3	4	5- least deprived	
N	160	41	40	34	29	16	
Age years	57.1 (16.9)	55.8 (8.6)	58.2 (15.7)	52.9 (16.3)	59.6 (15.2)	62.4 (19.1)	0.32
BMI kg/m^2	30.2 (7.7)	31.0 (7.7)	30.7 (8.7)	29.8 (8.7)	29.3 (5.6)	29.6 (6.1)	0.88
TLCO % pred	47.3 (22.1)	41.7 (16.7)	46.7 (22.6)	51.7 (23.7)	46.0 (22.3)	55.0 (27.6)	0.27
RAP mmHg	8.8 (5.5)	9.3 (5.7)	9.9 (5.8)	7.8 (4.5)	9.1 (4.4)	6.4 (7.0)	0.22
mPAP mmHg	50.9 (12.3)	50.1 (11.1)	51.7 (15.3)	52.9 (10.9)	51.4 (10.5)	45.8 (12.1)	0.40
PAWP mmHg	8.3 (3.7)	8.7 (3.6)	9.1 (4.5)	6.8 (3.5)	8.9 (3.2)	7.7 (2.9)	0.08
SvO_2 %	60.6 (9.4)	61.7 (9.0)	58.7 (10.0)	62.1 (7.9)	59.5 (10.4)	61.4 (9.5)	0.56
CO L/min	3.8 (1.3)	3.9 (1.2)	3.8 (1.3)	3.6 (1.5)	3.8 (1.3)	3.4 (0.9)	0.62
6MWD m	245 (120)	203 (110)	239 (111)	281 (115)	257 (125)	251 (151)	0.20
NTproBNP pg/ml median (IQR)	1544 (3447)	1566 (3038)	1585 (3511)	1508 (3159)	2657 (5880)	771 (3123)	0.61
CAMPHOR							
Composite Score	46.7 (16.8)	53.0 (19.5)	47.1 (15.7)	48.1 (16.7)	43.4 (17.3)	39.8 (16.8)	0.53
Symptoms	16.1 (6.2)	18.1 (6.4)	13.8 (7.2)	17.2 (5.6)	16.5 (5.8)	14.4 (5.9)	0.45
Activities	14.8 (6.7)	16.6 (6.9)	15.4 (6.5)	16.1 (6.2)	12.8 (6.5)	11.9 (8.0)	0.46
Quality of Life	13.8 (6.3)	15.5 (6.3)	15.3 (6.8)	14.3 (6.2)	8.5 (6.2)	11.5 (4.8)	0.30
WHO FC I/II, N (%)	26 (16)	3 (7)	6 (18)	9 (26)	6 (21)	2 (13)	0.23
WHO FC III/IV, N (%)	133 (84)	38 (93)	33 (82)	25 (74)	23 (79)	14 (87)	
Survival months	49.1 (49.9)	51.1 (54.3)	39.7 (42.2)	52.9 (50.2)	49.1 (45.2)	59.0 (49.9)	0.69
Deaths N (%)	80 (50)	23 (56)	21 (53)	11 (32)	14 (48)	11 (69)	0.12

All values mean (SD) except where otherwise indicated.

N – number, BMI – body mass index, TLCO – transfer factor, RAP – right atrial pressure, mPAP – mean pulmonary artery pressure, PAWP – pulmonary arterial wedge pressure, PVR – pulmonary vascular resistance, SvO_2 – mixed venous oxygen saturation, CO – cardiac output, 6MWD – six minute walk distance, NT-pro-BNP – N-terminal pro-B type natriuretic peptide, CAMPHOR - Cambridge Pulmonary Hypertension Outcome Review, FC – WHO functional class

*p-value for trend over quintiles

Table S8. Baseline characteristics for male subjects and across SIMD quintiles.

Variable	All Subjects	Deprivation Quintile					p-value*
		1- most deprived	2	3	4	5- least deprived	
N	120	26	27	20	18	29	
Age years	63.3 (16.7)	59.2 (15.4)	59.3 (16.1)	67.9 (16.2)	60.2 (19.3	69.7 (15.1)	**0.047**
BMI kg/m^2	26.6 (4.9)	26.5 (5.3)	28.2 (6.2)	27.3 (4.4)	26.1 (4.7)	24.7 (2.7)	**0.14**
TLCO % pred	39.2 (21.5)	37.0 (17.7)	42.9 (22.7)	33.1 (18.7)	43.1 (30.9)	39.2 (17.8)	0.61
RAP mmHg	8.8 (5.5)	9.3 (6.0)	9.9 (5.8)	7.8 (4.5)	9.1 (4.4)	6.4 (7.0)	0.22
mPAP mmHg	48.5 (13.0)	52.1 (15.6)	47.6 (14.2)	47.2 (8.2)	49.2 (10.9)	46.4 (13.1)	0.53
PAWP mmHg	7.4 (3.2)	7.0 (3.1)	7.8 (3.7)	7.5 (2.8)	8.6 (2.8)	6.6 (3.3)	0.31
SvO_2 %	60.8 (9.6)	61.6 (10.7)	60.7 (8.5)	62.7 (8.2)	56.8 (12.3)	61.0 (8.7)	0.47
CO L/min	3.7 (1.0)	3.7 (0.8)	3.6 (1.0)	3.8 (1.1)	3.8 (1.0)	3.6 (1.0)	0.89
6MWD m	267 (123)	266 (117)	296 (130)	250 (153)	274 (135)	250 (103)	0.80
NTproBNP pg/ml median (IQR)	1864 (3203)	1909 (3958)	2024 (3710)	1320 (1469)	1184 (2482)	3688 (2690)	0.39
CAMPHOR							
Composite Score	44.8 (16.7)	46.2 (15.2)	46.2 (16.8)	52.0 (19.2)	33.5 (16.8)	40.0 (17.5)	0.47
Symptoms	14.5 (5.9)	14.3 (5.5)	16.0 (5.8)	16.3 (7.5)	9.8 (4.8)	13.7 (5.9)	0.43
Activities	13.8 (6.3)	15.5 (6.3)	15.0 (6.8)	14.3 (6.2)	8.5 (6.2)	11.5 (4.8)	0.30
Quality of Life	16.4 (6.9)	16.3 (6.1)	15.2 (6.8)	21.3 (7.7)	15.3 (7.8)	14.5 (7.5)	0.43
WHO FC I/II, N (%)	22 (19)	5 (19)	6 (23)	2 (10)	3 (17)	6 (21)	0.82
WHO FC III/IV, N (%)	96 (81)	21 (81)	20 (77)	18 (90)	15 (83)	22 (79)	0.82
Survival months	35.6 (41.1)	46.2 (45.4)	40.6 (43.4)	19.6 (28.8)	28.6 (31.3)	36.3 (45.6)	0.23
Deaths N (%)	75 (63)	17 (65)	16 (59)	13 (65)	9 (50)	20 (69)	0.74

All values mean (SD) except where otherwise indicated.

N – number, BMI – body mass index, TLCO – transfer factor, RAP – right atrial pressure, mPAP – mean pulmonary artery pressure, PAWP – pulmonary arterial wedge pressure, PVR – pulmonary vascular resistance, SvO_2 – mixed venous oxygen saturation, CO – cardiac output, 6MWD – six minute walk distance, NT-pro-BNP – N-terminal pro-B type natriuretic peptide, CAMPHOR - Cambridge Pulmonary Hypertension Outcome Review, FC – WHO functional class

*p-value for trend over quintiles

Cox regression analysis looking at the association between deprivation quintile and all-cause mortality split by gender is shown in Tables S9 and S10, both univariate (unadjusted) and adjusted for time, age and sex. One result reached significance, namely deprivation quintile 3 when adjusted for time and age. However, as this was not part of a systematic trend, it is likely to be a chance event.

Table S9. Hazard ratios of all-cause mortality across SIMD quintiles for females both univariate analysis and adjusted for time, age and sex (N=160).

	Deprivation Quintile				
	1- most deprived	**2**	**3**	**4**	**5- least deprived**
HR, unadjusted	1.03	1.08	0.56	0.85	1.0 (ref)
95% Confidence Interval	0.49 – 2.16	0.59 – 2.29	0.24 – 1.32	0.38 – 1.91	
p-value	0.94	0.84	0.19	0.69	
HR, adjusted for time and age	1.28	1.14	0.77	0.86	1.0 (ref)
95% Confidence Interval	0.60 – 2.70	0.53 – 2.42	0.32 – 1.84	0.38 – 1.93	
p-value	0.53	0.74	0.56	0.71	

HR – hazard ratio

Table S10. Hazard ratios of all-cause mortality across SIMD quintiles for males both univariate analysis and adjusted for time, age and sex (N=120).

	Deprivation Quintile				
	1- most deprived	**2**	**3**	**4**	**5- least deprived**
HR, unadjusted	0.73	0.78	1.72	0.82	1.0 (ref)
95% Confidence Interval	0.38 – 1.40	0.40 – 1.51	0.85 – 3.48	0.37 – 1.81	
p-value	0.34	0.47	0.13	0.62	
HR, adjusted for time and age	1.52	1.09	3.17	1.54	1.0 (ref)
95% Confidence Interval	0.76 – 3.05	0.55 – 2.14	1.50 – 6.71	0.68 – 3.50	

p-value	0.24	0.80	**0.003**	0.30

HR – hazard ratio

Cox multivariate regression analysis was performed, looking for an association between deprivation quintile and all-cause mortality using Models 1 to 6 described previously. The results are summarized in Tables S11 and S12, showing only variables that reached signficance.

Table S11. Cox multivariate regression analysis of prediction of all-cause mortality in females by baseline variables (Models 1 to 6).

	N	**HR**	**95% Confidence Interval**	**p-value**
Model 1				
6MWD m	96	0.996	(0.992 – 0.999)	**0.049**
Model 2				
Age years	92	1.04	(1.01 - 1.07)	**0.005**
Model 3				
TLCO % pred	112	0.98	(0.96 – 1.00)	**0.014**
Model 4				
None	49			
Model 5				
None	49			
Model 6				
None	49			

N – number, HR – hazard ratio, BMI – body mass index, 6MWD – six minute walk distance, TLCO – transfer factor

Table S12. Cox multivariate regression analysis of prediction of all-cause mortality in males by baseline variables (Models 1 to 6).

	N	HR	95% Confidence Interval	p-value
Model 1				
Age years	78	1.08	(1.04 - 1.12)	**<0.001**
Model 2				
Age years	79	1.07	(1.03 - 1.11)	**0.001**
Log_{10}NTproBNP	79	2.01	(1.02 – 4.89)	**0.044**
Model 3				
Age years	89	1.06	(1.02 - 1.10)	**0.002**
TLCO % pred	89	0.97	(0.94 – 0.99)	**0.005**
Model 4				
Age years	38	1.18	(1.06 - 1.31)	**0.002**
BMI kg/m^2	38	1.18	(1.01 – 1.37)	**0.032**
Model 5				
Age years	38	1.16	(1.05 - 1.29)	**0.004**
BMI kg/m^2	38	1.18	(1.01 – 1.38)	**0.033**
Model 6				
Age years	38	1.19	(1.07 - 1.31)	**0.001**
BMI kg/m2	38	1.18	(1.02 – 1.37)	**0.030**

N – number, HR – hazard ratio, NT-pro-BNP – N-terminal pro-B type natriuretic peptide, TLCO – transfer factor, BMI – body mass index.