CAP 2 February 2018

(19 marks)

Please read the following abstract and tables and answer the questions based on this information and your other knowledge.

'Risk of mortality on and off methadone substitution treatment in primary care: a national … study

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ABSTRACT

Aim: To assess whether risk of death increases during periods of treatment transition, and investigate the impact of supervised methadone consumption on drug-related and all-cause mortality.

Design: National Irish study.

Setting: Primary care.

Participants: A total of 6983 patients on a national methadone treatment register aged 16–65 years between 2004 and 2010.

Measurement: Drug-related (primary outcome) and all-cause (secondary outcome) mortality rates and rate ratios for periods on and off treatment; and the impact of regular supervised methadone consumption.

Results: Crude drug-related mortality rates were 0.24 per 100 person-years on treatment and 0.39 off treatment, adjusted mortality rate ratio 1.63 [95% confidence interval (CI)=0.66–4.00]. Crude all-cause mortality rate per 100 person-years was 0.51 on treatment versus 1.57 off treatment, adjusted mortality rate ratio 3.64 (95% CI=2.11–6.30). All-cause mortality off treatment was 6.36 (95% CI=2.84–14.22) times higher in the first 2 weeks, 9.12 (95% CI=3.17–26.28) times higher in weeks 3–4, compared with being 5 weeks or more in treatment. All-cause mortality was lower in those with regular supervision (crude mortality rate 0.60 versus 0.81 per 100 person-years) although, after adjustment, insufficient evidence exists to suggest that regular supervision is protective (mortality rate ratio=1.23, 95% CI=0.67–2.27).

Conclusions: Among primary care patients undergoing methadone treatment, continuing in methadone treatment is associated with a reduced risk of death. Patients' risk of all-cause mortality increases following treatment cessation, and is highest in the initial 4-week period.'

Question 1 *(1 mark)*

Based on the abstract and your other knowledge, which option MOST accurately describes this study?

    A. Aetiology.

    B. Diagnostic categorization.

    C. Intervention.

    D. Observational.

    E. Prognostic.

    F. Qualitative.

    G. Screening intervention.

    H. Systematic review.

Question 2 *(1 mark)*

Based on the abstract and your other knowledge, which option MOST accurately describes this study population?

    A. Cluster sample.

    B. Probability sample.

    C. Purposive sample.

    D. Quota sample.

    E. Record linkage sample.

    F. Simple unrestricted random sample.

    G. Stratified sample.

Question 3 *(1 mark)*

Based on the abstract and your other knowledge, which option MOST accurately describes this study's method?

    A. Case Series.

    B. Cohort Study.

    C. Cross Over Study.

    D. Cross Sectional Study.

    E. Ecological Study.

    F. Experimental Study.

    G. Population Study.

    H. Randomised Controlled Study.

Question 4 *(1 mark)*

Based on the abstract and your other knowledge, which option MOST accurately describes the best study design to investigate the relationship between an unplanned exposure and an outcome?

A. Case Series.

B. Cohort Study.

C. Cross Over Study.

D. Cross Sectional Study.

E. Ecological Study.

F. Experimental Study.

G. Randomised Controlled Study.

Question 5 *(1 mark)*

Based on the abstract and your other knowledge, which option MOST accurately describes a study where each case acts as its own control?

- A. Case Series.
- B. Cohort Study.
- C. Cross Over Study.
- D. Cross Sectional Study.
- E. Ecological Study.
- F. Experimental Study.
- G. Randomised Controlled Study.

Question 6 *(1 mark)*

Based on the abstract and your other knowledge, which option describes the study method that would provide the MOST robust evidence of an association between methadone dosing and death in a cohort already in treatment?

    A. Case Series.

    B. Cohort Study.

    C. Cross Over Study.

    D. Cross Sectional Study.

    E. Ecological Study.

    F. Experimental Study.

    G. Randomised Controlled Study.

Question 7 *(2 marks)*

Table 1 Characteristics of patients and treatment episodes (abridged).

Characteristics	Alive	Dead	Number (%)[a]
Patients	n = 6770	n = 213	n = 6983
Male sex	4638 (65.8)	158 (74.2)	4796 (68.7)
Age (years) at start of study			
16–19	522 (7.7)	2 (0.9)	524 (7.5)
20–29	3452 (51.0)	67 (31.5)	3519 (50.4)
30–39	2137 (31.6)	83 (39.0)	2220 (31.8)
40–65	659 (9.7)	61 (28.6)	720 (10.3)
Total length of time on treatment			
Median	1114	744	1090 days
Range	14–2343 days	20–2315 days	14–2343 days
Mean (SD)	1195.7 (813.8)	805.5 (592.8)	1184 (810.7) days
Length of treatment episodes			
Median	85	60	83 days
Range	1–2343 days	1–2315 days	1–2343 days
Mean (SD)	169 (230.9)	123.8 (168.2)	168 (229.7) days
Median dose last treatment episode			
< 60 mg	2587 (38.2)	63 (29.6)	2650 (38.0)
60–120 mg	4016 (59.3)	144 (67.6)	4160 (59.6)
≥ 120 mg	167 (2.5)	6 (2.8)	173 (2.5)
Supervised methadone consumption			
≥ 50% prescriptions supervised	2766 (40.9)	57 (26.8)	2823 (40.4)
< 50% prescriptions supervised	4004 (59.1)	156 (73.2)	4160 (59.6)

[a] *Unless otherwise specified.*

Based on the abstract, Table 1 (abridged) and your other knowledge, which characteristic was associated with increased frequency of death compared to the remainder of their group?

    A. Aged 20-29.

    B. Female sex.

    C. Longer length of treatment episodes.

    D. Less than 50% of prescriptions supervised.

    E. Median dose of methadone < 60mgs.

Question 8 *(2 marks)*

Table 1 Characteristics of patients and treatment episodes (abridged).

Characteristics	Alive	Dead	Number (%)[a]
Patients	n = 6770	n = 213	n = 6983
Male sex	4638 (65.8)	158 (74.2)	4796 (68.7)
Age (years) at start of study			
16–19	522 (7.7)	2 (0.9)	524 (7.5)
20–29	3452 (51.0)	67 (31.5)	3519 (50.4)
30–39	2137 (31.6)	83 (39.0)	2220 (31.8)
40–65	659 (9.7)	61 (28.6)	720 (10.3)
Total length of time on treatment			
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Supervised methadone consumption			
≥ 50% prescriptions supervised	2766 (40.9)	57 (26.8)	2823 (40.4)
< 50% prescriptions supervised	4004 (59.1)	156 (73.2)	4160 (59.6)

Based on the abstract, Table 1 (abridged) and your other knowledge, which characteristic was associated with increased frequency of survival compared to the remainder of their group?

 A. Aged 30-39.

 B. Male sex.

 C. Longer length of treatment episodes.

 D. Less than 50% of prescriptions supervised.

 E. Median dose of methadone ≥60mgs.

Question 9 *(1 mark)*

Based on the abstract and your other knowledge, which option is a method of quantifying the increase in mortality of the study cohort with respect to the general population?

    A. Case Fatality Rate.

    B. Cause Specific Death Rate.

    C. Crude Mortality Rate.

    D. Mortality Rate Ratios.

    E. Proportionate Mortality Rate.

    F. Standardised Mortality Ratio.

Question 10 *(1 mark)*

Based on the abstract and your other knowledge, which option describes deaths from all causes for the study population?

A. Case Fatality Rate.

B. Cause Specific Death Rate.

C. Crude Mortality Rate.

D. Mortality Rate Ratios.

E. Proportionate Mortality Rate.

F. Standardised Mortality Ratio.

Question 11 *(1 mark)*

Based on the abstract and your other knowledge, which option describes deaths from drug related causes divided by the total number of deaths over the study period?

    A. Case Fatality Rate.

    B. Cause Specific Death Rate.

    C. Crude Mortality Rate.

    D. Mortality Rate Ratios.

    E. Proportionate Mortality Rate.

    F. Standardised Mortality Ratio.

Question 12 *(2 marks)*

Table 3 Crude and mortality rate ratios for all-cause mortality (abridged).

	Person-years	Death	Mortality /100 person-years	*Unadjusted analysis*		*Adjusted analysis*[a]	
				Mortality rate ratio (95% CI)	*P-value*	*Mortality rate ratio (95% CI)*	*P-value*
Overall on treatment	22 647.9	115	0.51	1.00	<0.001	1.00	<0.001
Overall off treatment	6247.4	98	1.57	3.09 (1.73–5.52)		3.64 (2.11–6.30)	
Remainder of time off treatment	5066.6	54	1.07	2.05 (1.48–2.86)		2.46 (1.28–4.37)	
Sex							
Female	9392.5	55	0.59	1.00	0.369	1.00	0.173
Male	19 502.8	158	0.81	1.38 (0.67–2.89)		1.54 (0.81–2.90)	
Age (years)							
16–19	1268.6	2	0.16	1.00	0.006	1.00	0.006
20–29	14 388.5	67	0.47	2.95 (0.12–74.10)		3.18 (1.21–49.20)	
30–39	9968.7	83	0.83	5.28 (0.21–131.31)		5.62 (1.36–86.82)	
40–65	3269.6	61	1.87	11.83 (0.47–298.27)		10.40 (4.66–164.52)	
Treatment episode							
First	6312.5	37	0.59	1.00	0.960	NA*	
Second	4510.4	31	0.69	1.17 (0.38–3.64)			
Third	3364.1	25	0.74	1.27 (0.38–4.23)			
Fourth	2614.9	20	0.76	1.30 (0.36–4.75)			
Fifth or above	12 093.5	100	0.83	1.41 (0.58–3.45)			
Median methadone dose (last treatment episode)							
< 60 mg/day	10 091.3	63	0.62	0.78 (0.58–1.05)	0.252	NA*	
60–120 mg/day	18 028.5	144	0.80	1.00			
≥ 120 mg/day	775.6	6	0.77	0.97 (0.34–2.19)			
Supervised consumption							
Yes	9574.5	57	0.60	1.00	0.044	1.00	0.500
No	19 320.9	156	0.81	1.36 (1.00–1.84)		1.23 (0.67–2.27)	
Antipsychotics							
No	22 696.6	152	0.67	1.00	0.298	NA*	
Yes	6198.8	61	0.98	1.47 (0.73–2.97)			

*NA = covariates that were not significant ($P > 0.05$) at the univariate level of analysis were not included in the multivariate model.
CI = confidence interval.
[a] = Adjusted for all other variables included in table apart from calendar year, treatment episode, median methadone dose, antipsychotics, benzodiazepines, opioid analgesics and antidepressants; adjusted rate ratios for variables other than on/off treatment are from model with treatment divided into specific periods.

Based on the abstract, Table 3 (abridged) and your other knowledge, what is the probability that the true crude mortality ratio for overall off treatment is less than 1.73?

A. 0.01

B. 0.025

C. 0.05

D. 0.075

E. 0.10

F. 0.125

Question 13 *(2 marks)*

Based on the abstract, Table 3 (abridged) and your other knowledge, which factor is associated with an increase in the crude mortality rate ratio?

Table 3 Crude and mortality rate ratios for all-cause mortality (abridged).

	Person-years	Death	Mortality /100 person-years	Unadjusted analysis Mortality rate ratio (95% CI)	P-value	Adjusted analysis[a] Mortality rate ratio (95% CI)	P-value
Overall on treatment	22 647.9	115	0.51	1.00	< 0.001	1.00	< 0.001
Overall off treatment	6247.4	98	1.57	3.09 (1.73–5.52)		3.64 (2.11–6.30)	
Remainder of time off treatment	5066.6	54	1.07	2.05 (1.48–2.86)		2.46 (1.28–4.37)	
Sex							
Female	9392.5	55	0.59	1.00	0.369	1.00	0.173
Male	19 502.8	158	0.81	1.38 (0.67–2.89)		1.54 (0.81–2.90)	
Age (years)							
16–19	1268.6	2	0.16	1.00	0.006	1.00	0.006
20–29	14 388.5	67	0.47	2.95 (0.12–74.10)		3.18 (1.21–49.20)	
30–39	9968.7	83	0.83	5.28 (0.21–131.31)		5.62 (1.36–86.82)	
40–65	3269.6	61	1.87	11.83 (0.47–298.27)		10.40 (4.66–164.52)	
Treatment episode							
First	6312.5	37	0.59	1.00	0.960	NA*	
Second	4510.4	31	0.69	1.17 (0.38–3.64)			
Third	3364.1	25	0.74	1.27 (0.38–4.23)			
Fourth	2614.9	20	0.76	1.30 (0.36–4.75)			
Fifth or above	12093.5	100	0.83	1.41 (0.58–3.45)			
Median methadone dose (last treatment episode)							
< 60 mg/day	10091.3	63	0.62	0.78 (0.58–1.05)	0.252	NA*	
60–120 mg/day	18028.5	144	0.80	1.00			
≥ 120 mg/day	775.6	6	0.77	0.97 (0.34–2.19)			
Supervised consumption							
Yes	9574.5	57	0.60	1.00	0.044	1.00	0.500
No	19 320.9	156	0.81	1.36 (1.00–1.84)		1.23 (0.67–2.27)	
Antipsychotics							
No	22 696.6	152	0.67	1.00	0.298	NA*	
Yes	6198.8	61	0.98	1.47 (0.73–2.97)			

*NA = covariates that were not significant ($P > 0.05$) at the univariate level of analysis were not included in the multivariate model.
CI = confidence interval.
[a] = Adjusted for all other variables included in table apart from calendar year, treatment episode, median methadone dose, antipsychotics, benzodiazepines, opioid analgesics and antidepressants; adjusted rate ratios for variables other than on/off treatment are from model with treatment divided into specific periods.

    A. Age.

    B. Median methadone dose.

    C. Gender.

    D. Treatment episode.

    E. Use of antipsychotics.

Question 14 *(1 mark)*

Based on the abstract and your other knowledge, the range of values within which the mortality rate ratio is estimated to lie is referred to as…

- **A.** Confidence Interval.
- **B.** Error Bars.
- **C.** Estimated Regression Coefficient.
- **D.** P Value.
- **E.** Standard Deviation.
- **F.** Standard Error.
- **G.** Analysis of Variance.

Question 15 *(1 mark)*

Based on the abstract and your other knowledge, which statistic or method can be used to measure the association of antipsychotic use to the likelihood of death as an outcome?

- **A.** Chi Square.
- **B.** Confidence Interval.
- **C.** Error Bars.
- **D.** Linear Regression.
- **E.** P Value.
- **F.** Standard Deviation.
- **G.** Standard Error.