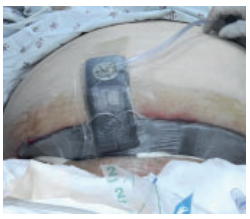
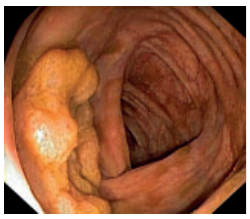
research



Negative pressure wound therapy and risk of surgical site infection p 187

Drug prophylaxis for covid-19 p 188

Survival from critical illness and risk of future suicide and deliberate self-harm p 189



Risk of CRC with family history of polyps in first degree relatives p 190

ORIGINAL RESEARCH Multicentre parallel group randomised controlled trial

Closed incision negative pressure wound therapy versus standard dressings in obese women undergoing caesarean section

Gillespie BM, Webster J, Ellwood D, et al

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Find this at: http://dx.doi.org/10.1136/bmj.n893

Study question Does prophylactic closed incision negative pressure wound therapy (NPWT) decrease the occurrence of surgical site infection compared with standard dressings in obese women undergoing caesarean section?

Methods This multicentre, randomised controlled trial took place in four Australian hospitals between October 2015 and November 2019. Eligible women with a pre-pregnancy body mass index of 30 or greater scheduled for caesarean section were randomised to closed incision NPWT or standard dressing. The primary outcome was 30 day incidence of surgical site infection. Secondary outcomes included depth of surgical site infection (superficial, deep, or organ/body space), rates of wound complications (dehiscence, haematoma, seroma, bleeding, bruising), length of stay in hospital, and dressing related adverse events.

Study answer and limitations Surgical site infection occurred in 75/1017 (7.4%) women treated with closed incision NPWT and in 99/1018 (9.7%) women treated with a standard dressing (risk ratio 0.76, 95% confidence interval 0.57 to 1.01; P=0.06). However, some surgical site infections might have been missed owing to lack of access to general practice data or if women attended a different hospital for treatment of a surgical infection.

What this study adds The results suggest a reduction in risk of surgical site infection when prophylactic closed incision NPWT is used rather than standard dressings for obese women after caesarean section. However, wider implementation of NPWT in this population needs to be balanced alongside the risk of blistering and cost effectiveness.

Funding, competing interests, and data sharing This trial was funded by the Australian National Health and Medical Research Council. The funders had no role in study design and implementation, data analysis, or interpretation of results. The authors declare no competing interests.

Access to patients' data is not available for this study; the published protocol can be found online at https://bmjopen.bmj.com/content/6/2/e010287.

Trial registration ANZCTR 12615000286549.

Clinical outcomes for intention to treat population with missing data on primary outcome (28 women) assumed to be no surgical site infection, conservatively favouring standard care. Values are numbers (percentages) unless stated otherwise

Clinical outcomes	All (n=2035)	Closed incision NPWT (n=1017)	Standard dressing (n=1018)	Relative risk (95% CI)	P value
SSI	174 (8.6)	75 (7.4)	99 (9.7)	0.76 (0.57 to 1.01)	0.06
Complications	247 (12.1)	123 (12.1)	124 (12.2)	0.99 (0.79 to 1.25)	0.95
Median (IQR) HLOS, days (n=2019)*	3.0 (2.0-4.0)	3.0 (2.0-4.0)	3.0 (2.0-4.0)	-	0.32
Readmissions	36 (1.8)	23 (2.3)	13 (1.3)	1.76 (0.90 to 3.46)	0.09
Pain*†	32 (1.6)	21 (2.1)	11 (1.1)	1.90 (0.92 to 3.93)	0.07
Reoperations*‡	9 (0.4)	4 (0.4)	5 (0.5)	0.80 (0.22 to 2.96)	0.75

HLOS=hospital length of stay; IQR=interquartile range; NPWT=negative pressure wound therapy; SSI=surgical site infection.
*Data not available for randomised patients withdrawn from study.
†Pain associated with surgical wound requiring readmission measured as binary variable (yes/no).
‡5 participants had reoperations for wound complications before hospital discharge.

Prophylaxis against covid-19

Bartoszko JJ, Siemieniuk RAC, Kum E, et al

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ROBIN UTRECHT/SHUTTERSTOCK

Study question What are the effects of drug prophylaxis on SARS-CoV-2 infection and covid-19?

Methods This living systematic review and network meta-analysis up to 25 March 2021 assessed randomised trials in which people at risk of covid-19 were assigned to prophylaxis or no prophylaxis (standard care or placebo). Pairs of reviewers independently screened potentially eligible articles. Random effects bayesian network meta-analysis was performed after duplicate data abstraction. Risk of bias of the included studies was assessed using a modification of the Cochrane risk of bias 2.0 tool, and the certainty of the evidence was assessed using the grading of recommendations assessment, development, and evaluation (GRADE) approach.

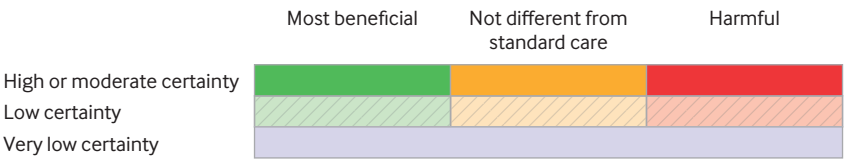
Study answer and limitations Hydroxychloroquine showed no important effect on admission to hospital (risk difference 1 fewer per 1000 participants, 95% credible interval 3 fewer to 4 more; high certainty) or mortality (1 fewer per 1000, 2 fewer to 3 more; high certainty). It probably has no important effect on laboratory confirmed SARS-CoV-2 infection (2 more per 1000, 18 fewer to 28 more; moderate certainty), probably increases the risk of adverse effects leading to drug discontinuation (19 more per 1000, 1 fewer to 70 more; moderate certainty), and might have no important effect on suspected, probable, or laboratory confirmed SARS-CoV-2 infection (15 fewer per 1000, 64 fewer to 41 more; low certainty). Because of serious risk of bias and very serious imprecision, it is highly uncertain whether ivermectin combined with iota-carrageenan and ivermectin alone reduce the risk of SARS-CoV-2 infection. Because conclusions for ivermectin are limited by very low certainty evidence, it is anticipated that future studies evaluating ivermectin for prophylaxis might substantially change the results.

What this study adds This, the first living systematic review and network meta-analysis on prophylaxis against covid-19, provides a comprehensive overview of the evidence for hydroxychloroquine and ivermectin prophylaxis, and directly informs the World Health Organization living guidelines on drugs to prevent covid-19. Hydroxychloroquine did not reduce rate of infection, hospital admission, or mortality, but more people stopped the drug because of adverse events. The studies on ivermectin so far have been small and therefore whether ivermectin reduces infection remains very uncertain. No other drug has been studied in large enough trials to make any inferences regarding the effects of prophylaxis on covid-19.

Systematic review registration This review was not registered. The protocol established a priori is included as a supplement with the full paper on bmj.com.

Funding, competing interests, and data sharing This study was supported by the Canadian Institutes of Health Research. See full paper on bmj.com for competing interests. No additional data available.

	Laboratory confirmed SARS-CoV-2 infection	Suspected, probable, or laboratory confirmed SARS-CoV-2 infection	Admission to hospital	Mortality	Adverse effects leading to drug discontinuation	Time to symptom resolution or clinical improvement
Standard care*	65 per 1000	167 per 1000	5 per 1000	3 per 1000	15 per 1000	
Hydroxychloroquine	2 (-18 to 28)†	-15 (-64 to 41)	-1 (-3 to 4)	-1 (-2 to 3)†	19 (-1 to 70)	
Ivermectin, iota-carrageenan	-52 (-58 to -37)					
Ivermectin	-50 (-59 to -16)	-159 (-165 to -144)		-1 (-3 to 68)†		



Summary of effects compared with standard care. *Row shows expected risk of each outcome with standard care. †Best estimate of effect was obtained from direct evidence. Empty cells indicate that no evidence was available for the specific intervention. Numbers in coloured cells are estimated risk differences (95% confidence intervals) per 1000 participants or mean differences (95% confidence intervals) in days compared with standard care

Suicide and self-harm in adult survivors of critical illness

Fernando SM, Qureshi D, Sood MM, et al

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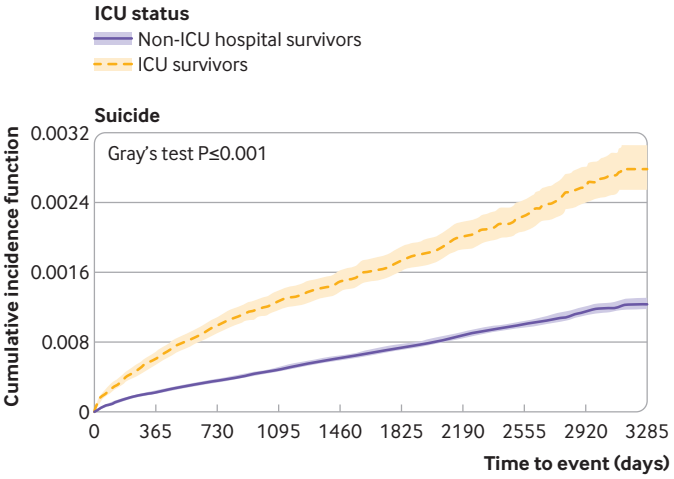
Study question What is the association between survival from critical illness and future suicide and deliberate self-harm?

Methods This population based cohort study identified consecutive adult survivors (≥18 years) of intensive care from Ontario, Canada, between January 2009 and December 2017. Patient characteristics and outcomes were obtained through linked and validated provincial databases. Intensive care unit (ICU) survivors were compared with hospital survivors who did not need ICU admission (non-ICU hospital survivors). The primary outcome was the composite of death by suicide (as noted in provincial death records) and deliberate self-harm events after discharge. Suicide and self-harm were also assessed independently. Incidence of suicide was evaluated while accounting for competing risk of death from other causes. Analyses were conducted by using overlap propensity score weighted, cause specific Cox proportional hazards models. Weights were calculated by using several variables, including age, sex, year of index admission, and number of hospital admissions in the past year. Prognostic factors associated with suicide and deliberate self-harm were identified among ICU survivors.

Study answer and limitations 423 060 consecutive ICU survivors (mean age 61.7 years, 39.1% women) were identified. During the study period, the crude incidence (per 100 000 person years) of suicide, self-harm, and the composite outcome among ICU survivors was 41.4, 327.9, and 361.0, respectively, compared with 16.8, 177.3, and 191.6 in non-ICU hospital survivors. Analysis using weighted models showed that ICU survivors (compared with non-ICU hospital survivors) had a higher risk of suicide (adjusted hazards ratio 1.22, 95% confidence interval 1.11 to 1.33) and self-harm (1.15, 1.12 to 1.19). Among ICU survivors, several factors were associated with suicide or self-harm: previous depression or anxiety (5.69, 5.38 to 6.02), previous post-traumatic stress disorder (1.87, 1.64 to 2.13), invasive mechanical ventilation (1.45, 1.38 to 1.54), and renal replacement therapy (1.35, 1.17 to 1.56). Because of the observational study design and despite trying to control for known and available confounders, a causal link between ICU survivorship and future suicide could not be confirmed.

What this study adds Survivors of critical illness have increased risk of suicide and self-harm, and these outcomes were associated with pre-existing psychiatric illness and receipt of invasive life support.

Funding, competing interests, and data sharing
This study was funded by the Institut du Savoir Montfort, Hôpital Montfort, Ottawa. Full funding and competing interests are in the full paper on bmj.com. Data access might be granted when prespecified criteria are met for confidential access.



Cumulative incidence function curve for suicide among intensive care unit (ICU) survivors and non-ICU hospital survivors

JOHN LAMPARSKI/NURPHOTO VIA GETTY IMAGES

Risk of colorectal cancer in first degree relatives of patients with colorectal polyps

Song M, Emilsson L, Roelstraete B, Ludvigsson JF

Cite this as: *BMJ* 2021;373:n877
Find this at: http://dx.doi.org/10.1136/bmj.n877

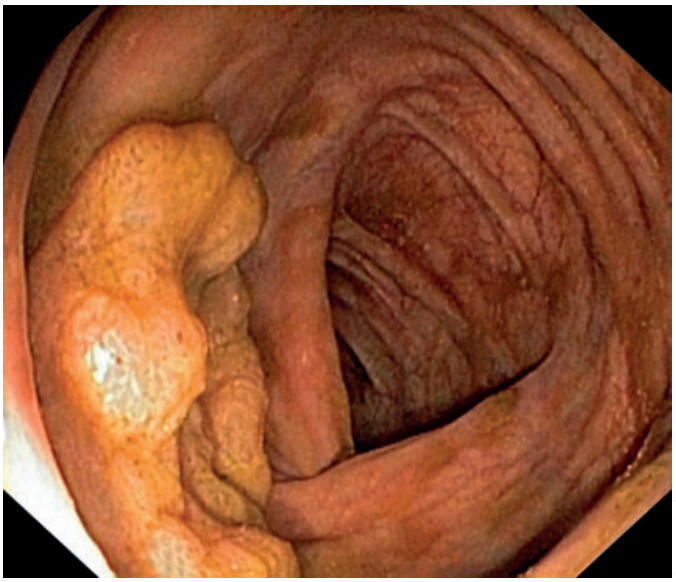
Study question What is the risk of colorectal cancer in first degree relatives of patients with precursor lesions for colorectal cancer?

Methods This case-control study assessed colorectal polyps in the first degree relatives (parents and full siblings) of 68 060 patients with colorectal cancer and 333 753 matched controls through linkage to the Swedish multi-generation register and gastrointestinal cohort of the Epidemiology Strengthened by histoPathology Reports in Sweden histopathology. Multivariable adjusted odds ratios for colorectal cancer were calculated according to the number of first degree relatives with a polyp and age at diagnosis of the polyp.

Study answer and limitations After adjusting for family history of colorectal cancer and other covariates, having a first degree relative with a polyp (8.4% (n=5742) in cases and 5.7% (n=18 860) in controls) was associated with a higher risk of colorectal cancer (odds ratio 1.40, 95% confidence interval 1.35 to 1.45). To put this risk in perspective, the age specific absolute risk of colon and rectal cancers was estimated according to family history of polyps based on the 2018 national incidence of colorectal cancer in Sweden. For example, the absolute risk of colon cancer in individuals aged 60-64 years with and without a family history of colorectal polyps was, respectively, 94.3 and 67.9 per 100 000 for men and 89.1 and 64.1 per 100 000 for women. The association between family history of polyps and risk of colorectal cancer was strengthened by the increasing number of first degree relatives with polyps (≥2 first degree relatives: 1.70, 1.52 to 1.90, P<0.001 for trend) and decreasing age at polyp diagnosis (<50 years: 1.77, 1.57 to 1.99, P<0.001 for trend). A particularly strong association was found for early onset colorectal cancer diagnosed before age 50 years (≥2 first degree relatives: 3.34, 2.05 to 5.43, P=0.002 for heterogeneity). The odds ratio for colorectal cancer in individuals who had one first degree relative with colorectal cancer but no polyps was 1.70 (1.65 to 1.76) and in those who had two or more first degree relatives with both polyps and colorectal cancer was 5.00 (3.77 to 6.63) (P<0.001 for interaction). This study lacked information on indications for endoscopic examination for polyp detection in first degree relatives.

What this study adds The findings suggest that early screening for colorectal cancer might be considered for first degree relatives of patients with polyps.

Funding, competing interests, and data sharing This work was supported by the National Institutes of Health and American Cancer Society. No competing interests relevant to this study. No additional data available.



CAMAL, ISM/SPL

Association between family history of polyps in first degree relatives and risk of colorectal cancer (CRC)

Polyp types	Cases (n=68 060)	Controls (n=333 753)	Age adjusted odds ratio (95% CI)*	Multivariable adjusted odds ratio (95% CI)†	Multivariable+family history of CRC adjusted odds ratio (95% CI)‡
No polyps	62 318 (91.6)	314 893 (94.3)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Any polyp	5742 (8.4)	18 860 (5.7)	1.55 (1.50 to 1.60)	1.62 (1.57 to 1.68)	1.40 (1.35 to 1.45)
Advanced polyps	2194 (3.2)	6477 (1.9)	1.68 (1.60 to 1.77)	1.76 (1.67 to 1.86)	1.44 (1.36 to 1.51)
Serrated polyps:					
Hyperplastic	1667 (2.4)	6114 (1.8)	1.34 (1.27 to 1.42)	1.38 (1.30 to 1.46)	1.23 (1.16 to 1.31)
Sessile serrated	123 (0.2)	437 (0.1)	1.37 (1.12 to 1.67)	1.43 (1.16 to 1.77)	1.27 (1.03 to 1.57)
Conventional adenomas:					
Tubular	2458 (3.6)	7783 (2.3)	1.57 (1.50 to 1.64)	1.62 (1.54 to 1.70)	1.39 (1.32 to 1.46)
Tubulovillous	1856 (2.7)	5437 (1.6)	1.69 (1.60 to 1.79)	1.77 (1.67 to 1.87)	1.44 (1.36 to 1.53)
Villous	252 (0.4)	697 (0.2)	1.77 (1.54 to 2.05)	1.82 (1.57 to 2.12)	1.40 (1.20 to 1.63)

*Conditional logistic regression was used to account for matching on age, sex, year of birth, and county of residence.
†Multivariable model was further adjusted for year of birth (continuous), family size (continuous), income levels (fifths), education (≤9 years, 10-12 years, >12 years, missing), total number of previous clinic visits (fifths), number of previous endoscopies (0, 1, 2, ≥3), Charlson comorbidity index score (continuous), and major comorbidities (all binary, including diabetes, cardiovascular disease, non-CRC, liver disease, chronic pulmonary disease, connective tissue disease, and peptic ulcer disease).
‡Further adjusted for family history of CRC in first degree relatives.