

Supplemental Online Content

Mueller TC, Kehl V, Dimpel R, et al; the IOWISI study group. Intraoperative wound irrigation for the prevention of surgical site infection after laparotomy: a randomized clinical trial by CHIR-Net. *JAMA Surg*. Published online February 21, 2024. doi:10.1001/jamasurg.2023.7985

eAppendix 1. CDC classification of intraoperative Level of Contamination (LOC)

eAppendix 2. CDC classification of Surgical Site Infection (SSI)

eTable 1. Sensitivity analysis of the primary endpoint with the subdistributional hazard model of Fine and Gray with SSI as main event, re-laparotomy and death as competing risks, treatment group, and several patient characteristics as covariates

eTable 2. Analysis of the primary endpoint with the subdistributional hazard model of Fine and Gray with SSI as main event and relaparotomy and death as competing risks, and treatment group, level of contamination, BMI class, cardiovascular, and pulmonary comorbidities as covariates

eTable 3. Frequency, severity, causal relationship, and types of serious adverse events for the wound irrigation groups PHX, saline, and no irrigation

eTable 4. Clavien–Dindo classification of surgical complications (including SSI I-III) in the IOWISI trial by study group

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. 1 CDC classification of intraoperative Level of Contamination (LOC)

LOC	Criteria	SSI rates*
Level I/ Clean	-uninfected operative wounds -no inflammation is encountered -the respiratory, alimentary, genital, or uninfected urinary tracts are not entered	1-5%
Level II/ Clean-contaminated	-the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination -no evidence of infection or major break in technique is encountered	3-11%
Level III/ Contaminated	-operations with major breaks in sterile technique or gross spillage from gastrointestinal tract -incisions in which acute, non-purulent inflammation is encountered -outside object had contact with wound (e.g., bullet, knife blade)	10-17%
Level IV/ Dirty-infected	- existing clinical infection -perforated viscera -foreign object lodged in wound -any wound that has been exposed to pus or fecal matter	>27%

*according to Reeves N, Torkington J. *Prevention of surgical site infections. Surgery (Oxford). 2022;40(1):20-4.*

eAppendix. 2 CDC classification of Surgical Site Infection (SSI)

Infection occurs within 30 days after the operation ...	
Superficial incisional SSI (class I)	...and infection involves only skin or subcutaneous tissue and at least <i>one</i> of the following: <ol style="list-style-type: none">1 Purulent drainage from the superficial incision2 Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision3 At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat <i>and</i> superficial incision is deliberately opened by surgeon, <i>unless</i> incision is culture negative
Deep incisional SSI (class II)	...and infection involves deep soft tissues (fascial and muscle layers) and at least <i>one</i> of the following: <ol style="list-style-type: none">1 Purulent drainage from the deep incision but not from the organ/space component of the surgical site2 A deep incision spontaneously dehisces or is deliberately opened by a surgeon3 And at least one of the following symptoms: fever (>38°C), localized pain, or tenderness of the incision area <i>unless</i> incision is culture negative4 An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination
Organ/space SSI (class III)	...and infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least <i>one</i> of the following: <ol style="list-style-type: none">1 Purulent drainage from a drain that is placed through a stab wound into the organ/space2 Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space
...or the infection is diagnosed by the attending surgeon	

eTable 1. Sensitivity analysis of the primary endpoint with the subdistributional hazard model of Fine and Gray with SSI as main event, re-laparotomy and death as competing risks, treatment group, and several patient characteristics as covariates

	95%CI for HR			
	HR	Lower	Upper	P-value
<i>Treatment group</i>				0.833
(Test 1) No irrigation vs. PHX	1.123	0.579	2.175	0.732
(Test 2) Saline vs. PHX	1.167	0.701	1.945	0.552
<i>Level of contamination</i>				
III/IV vs. I/II	1.396	0.565	3.450	0.469
<i>BMI class</i>				0.780
18.5 ≤ BMI < 25 (vs. BMI < 18.5)	1.339	0.371	4.830	0.656
25 ≤ BMI < 30 (vs. BMI < 18.5)	1.075	0.290	3.985	0.914
30 ≤ BMI (vs. BMI < 18.5)	1.022	0.260	4.012	0.975
<i>Diabetes</i>				
Yes vs. no	0.836	0.449	1.556	0.572
<i>NNIS risk score</i>	1.019	0.735	1.413	0.910
<i>Type of surgery</i>				0.267
HBP vs. colorectal	0.564	0.284	1.121	0.102
Upper GI vs. colorectal	0.559	0.253	1.235	0.151
Other vs. colorectal	0.284	0.037	2.148	0.223
<i>Duration of surgery (min)</i>	1.001	0.999	1.003	0.205
<i>Intraoperative change of gloves</i>				
Yes vs. no	1.076	0.637	1.818	0.783
<i>Use of wound edge protectors</i>				
Yes vs. no	1.094	0.635	1.887	0.746
<i>Enterostomy created</i>				
Yes vs. no	1.975	0.913	4.274	0.084

Abbreviations: PHX = Polyhexanide; BMI = body mass index; CI = Confidence interval; HR = Hazard ratio; HBP = hepatobiliary-pancreatic, GI = Gastrointestinal, NNIS = National Nosocomial Infections Surveillance

eTable 2. Analysis of the primary endpoint with the subdistributional hazard model of Fine and Gray with SSI as main event and relaparotomy and death as competing risks, and treatment group, level of contamination, BMI class, cardiovascular, and pulmonary comorbidities as covariates

	HR	95%CI for HR		P-value
		Lower	Upper	
<i>Treatment group</i>				
				0.714
(Test 1) No irrigation vs. PHX	1.236	0.635	2.404	0.533
(Test 2) Saline vs. PHX	1.201	0.740	1.950	0.458
<i>Level of contamination</i>				
III/IV vs. I/II	1.660	0.772	3.571	0.194
<i>BMI class</i>				
				0.829
18.5 ≤ BMI < 25 (vs. BMI < 18.5)	1.456	0.367	5.771	0.593
25 ≤ BMI < 30 (vs. BMI < 18.5)	1.197	0.305	4.699	0.797
30 ≤ BMI (vs. BMI < 18.5)	1.170	0.285	4.797	0.827
<i>Cardiovascular comorbidity</i>				
				0.562
Current (vs. none)	1.007	0.651	1.559	0.975
Previous (vs. none)	0.343	0.048	2.452	0.286
<i>Pulmonary comorbidity</i>				
				0.145
Current (vs. none)	0.829	0.385	1.782	0.630
Previous (vs. none)	2.135	0.966	4.718	0.061

Abbreviations: PHX = Polyhexanide; BMI = body mass index; CI = Confidence interval; HR = Hazard ratio

eTable 3. Frequency, severity, causal relationship, and types of serious adverse events for the wound irrigation groups PHX, saline, and no irrigation

	<i>Exposed to PHX n=291</i>			<i>Exposed to Saline n=295</i>			<i>Exposed to No irrigation n=103</i>			<i>P-value &</i>
	<i>Subjects affected</i>			<i>Subjects affected</i>			<i>Subjects affected</i>			
	<i>Events</i>	<i>n</i>	<i>(%)</i>	<i>Events</i>	<i>n</i>	<i>(%)</i>	<i>Events</i>	<i>n</i>	<i>(%)</i>	
				177				4	(40)	
SAE	178 (100)	95	(33)	(100)	104	(35)	63 (100)	1)	0·232
Severity (n, % #)										0·031
<i>Mild</i>	17 (9·6)	9 (5·1)	7 (11·1)
<i>Moderate</i>	48 (27·0)	54 (30·5)	14 (22·2)
<i>Severe</i>	58 (32·6)	65 (36·7)	28 (44·4)
<i>Life-threatening</i>	47 (26·4)	32 (18·1)	8 (12·7)
<i>Death</i>	8 (4·5)	17 (9·6)	6 (9·5)
Causal relationship (n, % #)										0·709 §
<i>Unrelated</i>	167 (93·8)	165 (93·2)	63 (100·0)
<i>Unlikely related</i>	11 (6·1)	11 (6·2)	0
<i>Probably related</i>	0	1 (0·6)	0
SAE specification*										
<i>Cardiac disorder</i>	6	5	(2)	6	4	(1)	3	3	(3)	0·583
<i>Respiratory, thoracic, or mediastinal disorder</i>	16	12	(4)	12	11	(4)	4	3	(3)	0·856
<i>Vascular disorder</i>	10	10	(3)	12	9	(3)	3	3	(3)	0·951
<i>Surgically relevant</i>	6	6	(2)	10	8	(3)	3	3	(3)	0·835
<i>Renal or urinary disorder</i>	3	3	(1)	2	2	(1)	2	2	(2)	0·553
<i>Gastrointestinal disorder</i>	30	24	(8)	32	31	(11)	14	1	(14 4)	0·279
<i>Surgically relevant</i>	15	13	(4)	17	17	(6)	8	8	(8)	0·419
<i>Intra-abdominal hemorrhage/hematoma</i>	5	5	(2)	3	3	(1)	4	4	(4)	0·158
<i>Hepatobiliary disorder</i>	10	10	(3)	18	13	(4)	4	4	(4)	0·815
<i>Surgically relevant</i>	5	5	(2)	0	0		1	1	(1)	0·222
<i>Infection or infestation</i>	24	24	(8)	26	24	(8)	6	6	(6)	0·712
<i>Surgically relevant</i>	11	11	(4)	17	17	(6)	5	5	(5)	0·494

<i>Injury, poisoning, or procedural complications</i>	30	26 (9)	31	30 (10)	14	1 (3)	0.560
<i>Surgically relevant</i>	28	25 (9)	29	28 (9)	14	1 (3)	0.489
<i>Anastomotic complications</i>	14	14 (5)	15	15 (5)	10	1 (10)	0.154
<i>Wound complications</i>	10	9 (3)	11	10 (3)	3	3 (3)	0.966
<i>Other</i>	49	32 (11)	38	28 (9)	13	1 (10)	0.823

Symbols: & χ^2 test over all groups, unless otherwise stated; § Fisher exact test comparing all groups; * coded with MedDRA; #

Number of SAE in the denominator

Abbreviations: PHX = Polyhexanide; SAE = Serious Adverse Event

eTable 4. Clavien–Dindo classification of surgical complications (including SSI I-III) in the IOWISI trial by study group

		Treatment group					
		PHX		Saline		No irrigation	
		N	%	N	%	N	%
Clavien– Dindo classification	Grade I	88	40,4%	84	35,1%	34	45,3%
	Grade II	38	17,4%	36	15,1%	7	9,3%
	Grade IIIa	52	23,9%	64	26,8%	16	21,3%
	Grade IIIb	37	17,0%	41	17,2%	16	21,3%
	Grade IVa	1	0,5%	3	1,3%	0	
	Grade IVb	1	0,5%	4	1,7%	0	
	Grade V	1	0,5%	7	2,9%	2	2,7%

Abbreviations: PHX = Polyhexanide