Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work. Supplement to:

Mohamed Abbas, Nathalie Vernaz, Elodie von Dach, Nicolas Vuilleumier, Stephan Harbarth, Benedikt D. Huttner. **Impact of restricting procalcitonin measurements in a Swiss tertiary-care hospital on antibiotic use, clinical outcomes and costs: an interrupted time-series analysis**

Contents

Geneva University Hospitals Infectious Diseases Guidance on Use of Procalcitonin

Procalcitonin (PCT) has been used in our hospital since 2009, and in the period before the intervention, the Infectious Diseases Department issued guidance in the form of an algorithm on use of PCT based on knowledge from the literature [1-4]. This was mainly for use in patients with either COPD exacerbations or sepsis/septic shock (some complicated infections such as endocarditis, *Staphylococcus aureus* bloodstream infection, etc. were excluded from the algorithm). For the latter, it was recommended to measure PCT on the first day of presentation, and a repeat dosage on day 5. If the PCT had decreased by ≥90%, we recommended discontinuing antibiotics if this was coherent with clinical evolution. If PCT had not decreased by ≥90% of baseline value, we recommended repeat measurements every 48 hours until it did. This guidance was present in our institution's antibiotic guide. Our antimicrobial stewardship team did not systematically review patients for whom PCT was measured, even if patients had low PCT levels and continued receiving antibiotics. Our facility has an antibiotic stewardship program with review of all positive blood cultures and review of antibiotic treatment in certain wards (e.g. intensive care unit). There is a list of "restricted" antibiotics, but this is a "soft" restriction in the sense that infectious diseases approval is not mandatory.

References

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2. Harbarth S, Holeckova K, Froidevaux C, Pittet D, Ricou B, Grau GE, et al. Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis. Am J Respir Crit Care Med. 2001;164(3):396-402.
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4. de Jong E, van Oers JA, Beishuizen A, Vos P, Vermeijden WJ, Haas LE, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. Lancet Infect Dis. 2016;16(7):819-27.

Supplementary Table 1 - Monthly numbers of procalcitonin (PCT) dosages, interrupted time series analysis (ITSA) model estimates, expected numbers of PCT dosages in absence of intervention, and antibiotic consumption rates (measured in defined daily doses [DDD])

Year	Month	Observed no. of PCT dosages	Predicted no. of PCT dosages (ITSA model)	Expected no. of PCT dosages (in absence of intervention)*	95% confidence interval for expected no. of PCT dosages	Antibiotic use (DDD/1000 patient-days)
2014	January	593	623.60	-	-	459.67
	February	613	625.38	-	-	467.87
	March	605	627.17	-	-	429.65
	April	650	628.95	-	-	441.42
	May	599	630.73	-	-	431.35
	June	558	632.51	-	-	405.52
	July	547	634.30	-	-	406.68
	August	461	636.08	-	-	425.13
	September	526	637.86	-	-	453.46
	October	544	639.64	-	-	435.33
	November	449	641.43	-	-	446.41
	December	532	643.21	-	-	482.61
2015	January	556	644.99	-	-	519.49
	February	584	646.77	-	-	545.09
	March	586	648.56	-	-	497.96
	April	535	650.34	-	-	470.83
	May	550	652.12	-	-	480.10
	June	623	653.90	-	-	491.47
	July	555	655.68	-	-	501.63
	August	737	657.47	-	-	511.62
	September	830	659.25	-	-	518.05
	October	817	661.03	-	-	477.78

Year	Month	Observed no. of PCT dosages	Predicted no. of PCT dosages (ITSA model)	Expected no. of PCT dosages (in absence of intervention)*	95% confidence interval for expected no. of PCT dosages	Antibiotic use (DDD/1000 patient-days)
	November	703	662.81	-	-	455.31
	December	771	664.60	-	-	521.16
2016	January	791	666.38	-	-	592.12
	February	111	30.80	668.16	535.18-801.13	525.07
	March	80	32.53	669.94	530.80-809.07	501.19
	April	68	34.27	671.73	526.32-817.11	482.97
	May	62	36.00	673.51	521.76-825.24	435.94
	June	65	37.73	675.29	517.13-833.43	483.27
	July	70	39.46	677.07	512.44-841.69	526.64
	August	46	41.19	678.86	507.69-850.01	508.48
	September	31	42.92	680.64	502.89-858.37	502.89
	October	66	44.66	682.42	498.05-866.78	481.39
	November	60	46.39	684.20	493.16-875.23	456.15
	December	68	48.12	685.99	488.24-883.72	525.70
2017	January	81	49.85	687.77	483.29-892.24	493.41
	February	70	51.58	689.55	478.30-900.79	504.94
	March	70	53.31	691.33	473.29-909.36	583.48
	April	73	55.05	693.11	468.26-917.96	524.20
	May	81	56.78	694.90	463.20-926.58	474.55
	June	63	58.51	696.68	458.13-935.22	470.20
	July	64	60.24	698.46	453.03-943.88	521.19
	August	68	61.97	700.24	447.92-952.56	499.57
	September	61	63.70	702.03	442.79-961.25	460.43
	October	48	65.43	703.81	437.65-969.96	504.76
	November	60	67.17	705.59	432.50-978.68	520.91

Year	Month	Observed no. of PCT dosages	Predicted no. of PCT dosages (ITSA model)	Expected no. of PCT dosages (in absence of intervention)*	95% confidence interval for expected no. of PCT dosages	Antibiotic use (DDD/1000 patient-days)
	December	57	68.90	707.37	427.33-987.41	546.01
2018	January	52	70.63	709.16	422.15-996.16	530.81
	February	60	72.36	710.94	416.96-1004.91	521.25
	March	79	74.09	712.72	411.76-1013.68	584.46
	April	84	75.82	714.50	406.55-1022.45	536.20
	May	70	77.56	716.29	401.33-1031.23	507.55

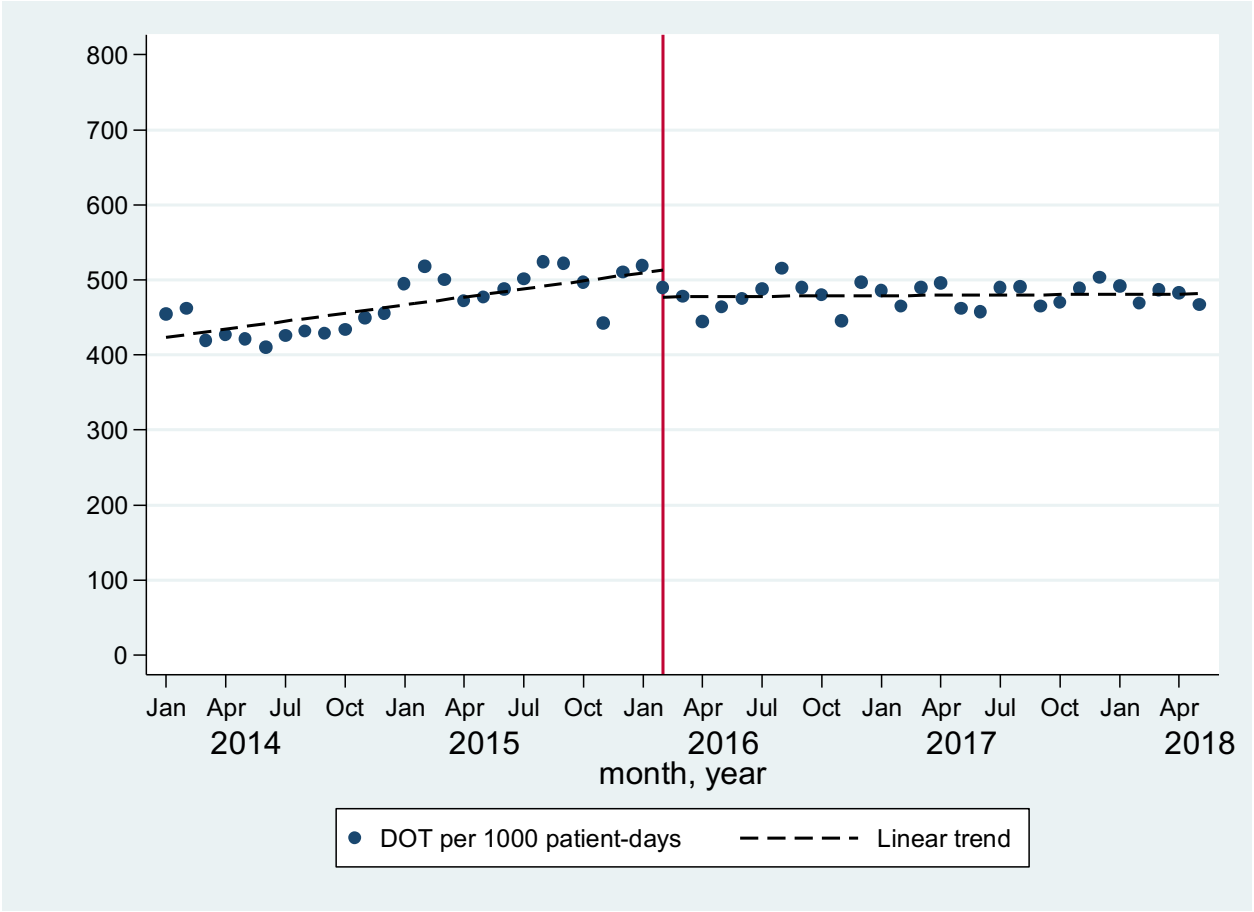
DDD, defined daily dose; ITSA, interrupted time-series analysis; PCT, procalcitonin

* if intervention hadn't taken place (i.e. *expected* values)

Supplementary Table 2 – Results of interrupted time-series evaluating the impact of discontinuation of procalcitonin dosage on number of procalcitonin measurements, incidence density of procalcitonin measurements (per 1000 patient-days), antibiotic consumption measured by DDD and DOT per 1000 patient-days, hospital length of stay, and in-hospital mortality.

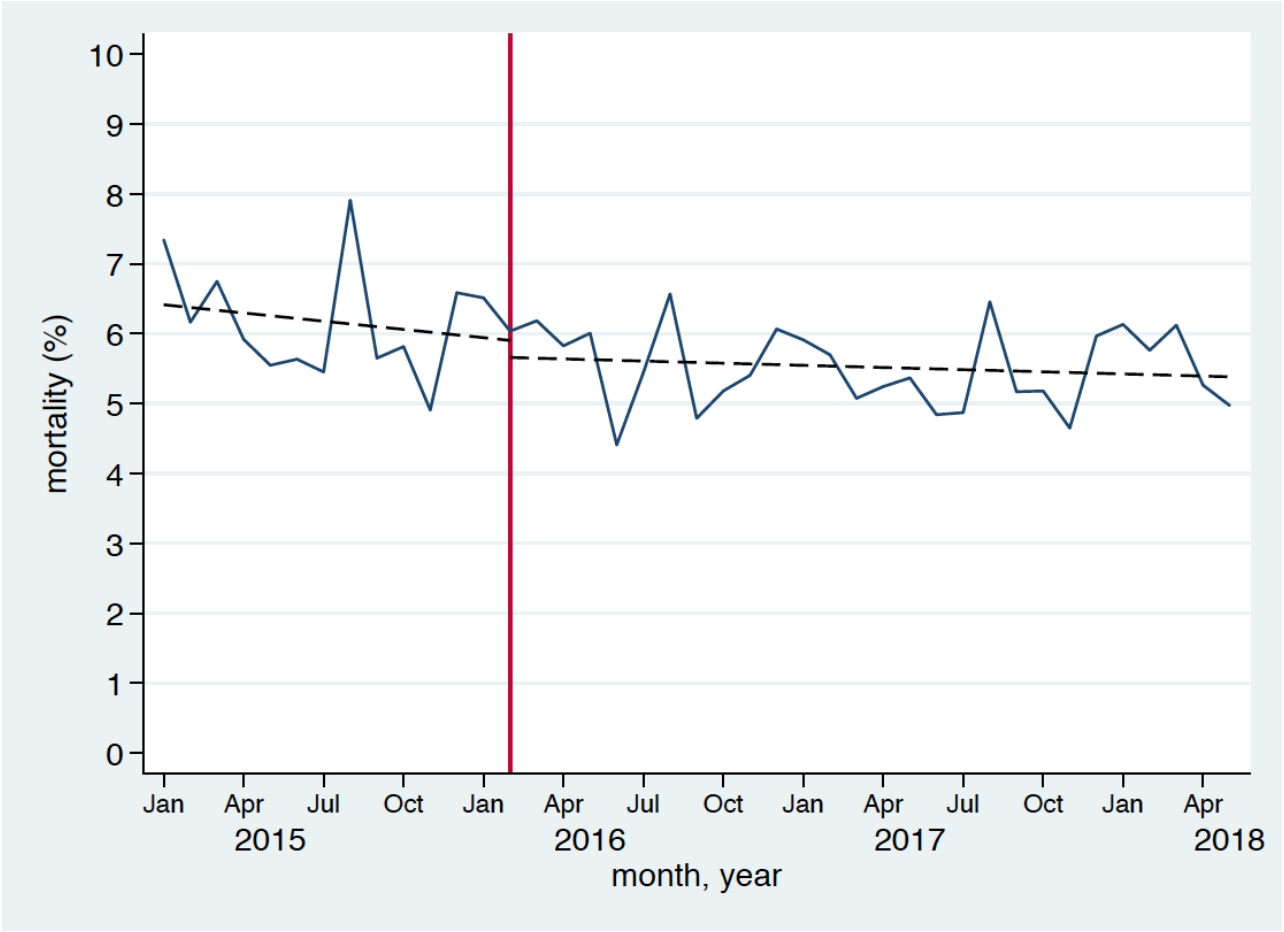
	Coefficient	**95% confidence interval**	***p*-value**
Number of PCT dosages			
Constant	602.21	509.45 to 694.97	<0.001
Slope before intervention	1.78	-2.37 to 5.93	0.39
Change in level	-637.36	-734.99 to -539.73	<0.001
Change in slope after intervention	-0.05	-8.18 to 8.08	0.99
Post-intervention linear trend	1.73	-1.49 to 4.95	0.29
Antibiotic consumption, DDD/1000 patient-days			
Constant	425.34	391.63 to 459.04	<0.001
Slope before intervention	4.25	1.43 to 7.07	0.004
Change in level	-47.28	-95.56 to 1.00	0.06
Change in slope after intervention	-2.61	-6.21 to 0.98	0.15
Post-intervention linear trend	1.64	-0.23 to 3.50	0.08
Antibiotic consumption, DOT/1000 patient-days			
Constant	424.52	397.43 to 451.61	<0.001
Slope before intervention	3.62	1.50 to 5.73	0.001
Change in level	-36.55	-70.34 to -2.76	0.04
Change in slope after intervention	-3.55	-6.05 to -1.04	0.006
Post-intervention linear trend	0.06	-0.95 to 1.08	0.90
Hospital length of stay, days			
Constant	4.88	4.58 to 5.19	<0.001
Slope before intervention	-0.02	-0.04 to 0.01	0.13
Change in level	-0.44	-0.70 to -0.18	0.001
Change in slope after intervention	0.01	-0.01 to 0.004	0.39
Post-intervention linear trend	-0.005	-0.01 to 0.004	0.28
In-hospital mortality, per 100 admissions			
Constant	6.43	5.72 to 7.15	<0.001
Slope before intervention	-0.04	-0.15 to 0.06	0.41
Change in level	-0.20	-1.26 to 0.86	0.71
Change in slope after intervention	0.03	-0.08 to 0.15	0.54
Post-intervention linear trend	-0.01	-0.04 to 0.02	0.46

Supplementary Figure 1 - Changes in monthly rate of antibiotic use (measured in days of therapy [DOT]) before and after discontinuation of procalcitonin measurements.



Supplementary Figure 2 – Changes (A) in-hospital mortality and (B) hospital length of stay (LOS) before and after discontinuation of procalcitonin dosages

A



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