Original article

Correlation between giving total parenteral nutrition via peripheral vascular access device and candidemia

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Abstract:

Background: *Candidemia has been the most common cause of fungal infection in hospitals, which is a problem worldwide. Some of the risk factors were prolonged use of antibiotics, central venous catheter insertion, use of total parenteral nutrition, etc. However, most of the candidemia risk factor studies used parenteral nutrition (PN) via a central venous catheter, and the risk of using PN via peripheral vascular access was inconclusive.* ***Objectives:*** *To study the relationship between using PN via peripheral vascular access and candidemia in hospitalized patients.* ***Methods:*** *Analytic observational, retrospective matching case-control study. We collected data from the ICU at Phramongkutklao Hospital from 1 January 2016 to 30 September 2020 and use the STATA14 program for analysis.* ***Results:*** *There were 42 patients in the disease group and 84 in the control group. The mean age of the patients was 65-year-old. The risk factors of candidemia included Prolonged antibiotic use (OR 5.01, 95CI: 1.37-18.34, p-value 0.015), using PN (OR 2.20, 95CI: 1.03-4.69, p-value 0.041), and using PN via central vascular access (OR 3.46, 95CI 1.10-10.88, p-value 0.034), but using TPN via peripheral vascular access is not a risk factor (OR 2.11, 95CI: 0.43-10.33, p-value 0.358). Using PN via peripheral vascular access over central venous catheter did not reduce candidemia risk (HR 0.88, 95CI: 0.36-2.15, p-value 0.78).* ***Conclusion:*** *Candidemia were associated with prolonged use of antibiotics, using PN, and using PN via a central venous catheter, but not with using PN via peripheral vascular access, as shown from the study. Nevertheless, using the PN via peripheral venous access over a central venous catheter did not decrease the risk of candidemia.*

Keywords: ● *Candidemia* ● *Total parenteral nutrition* ● *Peripheral parenteral nutrition*

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นิพนธ์ต้นฉบับ

ความสัมพันธ์ระหว่างการให้อาหารทางหลอดเลือดดำผ่านทางหลอดเลือดดำส่วนปลาย และการติดเชื้อราแคนดิดาในกระแสเลือด

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บทคัดย่อ

บทนำ *การติดเชื้อราแคนดิดาในกระแสเลือดพบได้บ่อยโดยมีอัตราการเสียชีวิตมากถึงร้อยละ 40 โดยมีปัจจัยเสี่ยง อาทิเช่น ได้รับยาปฏิชีวนะเป็นเวลานาน ได้รับการใส่สายสวนในหลอดเลือดดำใหญ่ และการให้สารอาหารทางหลอดเลือดดำ เป็นต้น อย่างไรก็ตาม การศึกษาหาปัจจัยเสี่ยงส่วนใหญ่ได้ทำการศึกษาโดยให้สารอาหารทางหลอดเลือดดำผ่านทางหลอดเลือดดำใหญ่ จึงเป็นคำถามของการวิจัยนี้*

วัตถุประสงค์ *เพื่อศึกษาความสัมพันธ์ระหว่างการให้อาหารทางหลอดเลือดดำผ่านทางหลอดเลือดดำส่วนปลายและการติดเชื้อราแคนดิดาในกระแสเลือด ในผู้ป่วยที่นอนโรงพยาบาล* ***วิธีดำเนินการวิจัย*** *การศึกษาจับคู่โรคโดยเก็บข้อมูลจากหอผู้ป่วยหนัก ในโรงพยาบาลพระมงกุฎเกล้า ตั้งแต่ 1 มกราคม 2559 ถึง 30 กันยายน 2563 โดยเก็บข้อมูลที่ต้องการศึกษาวิเคราะห์ผ่านโปรแกรม STATA14*

ผลการวิจัย *มีผู้ป่วย 42 คน ในกลุ่มโรค และ 84 คน ในกลุ่มควบคุม โดยมีอายุเฉลี่ย 65 ปี โดยปัจจัยเสี่ยงของการติดเชื้อราแคนดิดาในกระแสเลือดได้แก่ การได้รับยาปฏิชีวนะเป็นเวลานาน OR 5.01 (95CI: 1.37-18.34, p-value 0.015) การได้รับสารอาหารทางหลอดเลือดดำรวมผ่านทุกช่องทาง OR 2.20 (95CI: 1.03-4.69, p-value 0.041) และการได้รับสารอาหารผ่านทางหลอดเลือดดำใหญ่ OR 3.46 (95CI: 1.10-10.88, p-value 0.034), การได้รับสารอาหารทางหลอดเลือดดำผ่านทางหลอดเลือดดำส่วนปลายเทียบกับการให้ผ่านทางหลอดเลือดดำใหญ่สัมพันธ์กับการติดเชื้อราแคนดิดาในกระแสเลือดไม่ต่างกัน (HR 0.88, 95CI: 0.36-2.15, p-value 0.78)*

สรุป *จากการศึกษาพบว่า การได้รับยาปฏิชีวนะเป็นเวลานาน การได้รับสารอาหารทางหลอดเลือดดำรวมผ่านทุกช่องทาง และผ่านทางหลอดเลือดดำใหญ่ สัมพันธ์กับการติดเชื้อราแคนดิดาในกระแสเลือด แต่การได้รับสารอาหารผ่านทางหลอดเลือดดำส่วนปลายไม่สัมพันธ์กับการติดเชื้อราแคนดิดาในกระแสเลือด นอกจากนั้นการได้รับสารอาหารทางหลอดเลือดดำส่วนปลายไม่ลดอัตราการติดเชื้อราแคนดิดาอย่างมีนัยสำคัญทางสถิติเทียบกับการได้รับสารอาหารทางหลอดเลือดดำใหญ่*

คำสำคัญ: ● *ติดเชื้อแคนดิดาในกระแสเลือด* ● *การให้สารอาหารทางหลอดเลือดดำ*
● *การให้สารอาหารทางหลอดเลือดดำส่วนปลาย*

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Introduction

In hospitals, candidemia is the most common cause of fungal infection. With a mortality rate of over 40% and an increase in drug-resistant species, candidemia has become a problem in every healthcare setting around the world.[1]

Illness disrupting body metabolism, reduced appetite, and increased risk of malnutrition, which was found in 20-40% of hospital patients, complicate physician treatments.[2] Nutritional supplements were used to help malnourished patients improve their nutrition. Parenteral nutrition (PN) refers to the administration of nutrients such as protein, carbohydrates, lipids, minerals, and vitamins to patients who are unable to eat and require nutritional support.[3]

Candidemia risk factors include being admitted to the intensive care unit, receiving an immunosuppressive drug, prolonged use of antibiotics, inserting a central venous catheter, and using total parenteral nutrition, etc.[1]

Many studies have linked receiving parenteral nutrition through a central venous catheter to candidemia[4-10], and one study by Luszzati R, et al.[11] found that receiving parenteral nutrition through a peripheral vein was an independent risk factor for candidemia, which was explained by Swindell K, et al.[12] that candida biofilms formed by fungi respond to lipid and carbohydrate compounds in parenteral nutrition, as well as decreased intestinal movement, resulting in fungal translocation to the bloodstream.

The majority of the candidemia risk factor studies, on the other hand, used PN through a central venous catheter, and the risk of using PN through peripheral vascular access was limited and inconclusive. As a result, this research was conducted.

Objectives

To study the relationship between using PN via peripheral vascular access and candidemia in hospitalized patients, as well as to identify and prevent possible risk factors for candidemia, such as the amount of PN calories given, PN nutrient compounds, and PN type.

Methods

Study design and study population

The study was an analytic observational, retrospective matching case-control study. From 1 January 2016 to 30 September 2020, we collected data from the ICU at Phramongkutklao Hospital, a university-based hospital.

This research was approved by the Institutional Review Board (Royal Thai Army Medical Department) with the code number R208h63 on November 13, 2020.

Data collection:

The researchers gathered demographic information, potential risk factors, routes, total calories, and nutrient compositions in PN using the patients' ICD-10-TM code as an inclusion criterion, excluding patients under the age of 18 and those who did not have an ICD-10-TM code in the hospital computer systems.

The disease group were defined by patient with ICD-10-TM coding of B37.7 Candidal sepsis, B37.1 Pulmonary candidiasis, B37.5 Candidal meningitis, B37.6 Candidal endocarditis, and had hemoculture growth candida spp. as a definition of candidemia.

The control group, which included patients who did not meet the candidemia definition, was matched in a 1:2 (Disease:Control) ratio, with matching criteria including gender, age (over or under 5 years old), admission year, and ICU type.

Statistical analysis:

The number of exposures, cases, and controls were calculated using table 2x2 from Luzzati R, et al.[11], the minimum number of patients with shown significance was 24 in the disease group and 48 in the control group. The numerical data was displayed in proportionate, percentage, mean, median, and mode. Data relationships between the two groups were found using the odd ratio. In qualitative data, the Chi-square test or Fisher's exact test was used, and in continuous data, the independent t-test or Mann-Whitney U test was used. If the p-value was equal to or less than 0.05, differences were considered significant. The STATA14 program was used to analyze this study.

Result

There were 42 patients in the disease group and 84 in the control group. The patient was 65 years old on average. The majority of patients (68%) were male, admitted to Medical ICU (85.7%), used the civil servant medical scheme (70.6%), died in hospital (81%) and had a mean length of stay of 28.4 days. Patients in both groups had hypertension (68.3%), diabetes mellitus (31.7%), and dyslipidemia (50.8%) as underlying diseases, but patients in the control group had more chronic kidney disease (31% vs 21.4%) and solid malignancy (28.6% vs 9.5 %). (Table 1)

The prevalence of candidemia risk factors was shown in Table 2.

Table 1 Demographic data

Demographic	Total n (%)†	Candidemia n (%)†	Non Candidemia n (%)†
Overall‡	126 (100)	42 (33.3)	84 (66.7)
Age (Year)			
Mean (SD)	65.9 (5.9)	66.1 (6.4)	65.8 (5.2)
Median (IQR)	67.0 (57.0-78.0)	71.0 (58.0-78.0)	66.0 (56.0-78.5)
Min-Max	20-93	20-87	24-93
Gender			
Female	40 (31.7)	14 (33.3)	26 (31.0)
Male	86 (68.3)	28 (66.7)	58 (69.0)
Ward			
Medicine	108 (85.7)	36 (85.7)	72 (85.7)
Others	18 (14.3)	6 (14.3)	12 (14.3)
Health Insurance			
Civil servant medical scheme	89 (70.6)	28 (66.7)	61 (72.6)
Universal coverage	26 (20.6)	12 (28.6)	14 (16.7)
Self payment	3 (2.4)	1 (2.4)	2 (2.4)
Social security scheme	8 (6.4)	1 (2.3)	7 (8.3)
Drugs (items)			
Mean (SD)	5.7 (3.7)	5.5 (3.6)	5.8 (3.8)
Median (IQR)	5.5 (3.0-8.0)	6.0 (3.0-8.0)	5.0 (3.0-8.5)
Min-Max	0-16	0-13	0-16
Death			
No	24 (19.0)	6 (14.3)	18 (21.4)
Yes	102 (81.0)	36 (85.7)	66 (78.6)

Table 1 Demographic data (continue)

Demographic	Total n (%)†	Candidemia n (%)†	Non Candidemia n (%)†
Length of stays			
Mean (SD)	28.4 (30.1)	45.5 (41.4)	19.8 (17.3)
Median (IQR)	18.0 (11.0-36.0)	35.0 (18.0-57.0)	14.5 (8.0-24.5)
Min-Max	0-241	6-241	0-81
Hypertension			
No	40 (31.7)	11 (26.2)	29 (34.5)
Yes	86 (68.3)	31 (73.8)	55 (65.5)
Diabetes mellitus			
No	86 (68.3)	28 (66.7)	58 (69.0)
Yes, no insulin injection	29 (23.0)	12 (28.6)	17 (20.2)
Yes, insulin injection	11 (8.7)	2 (4.7)	9 (10.8)
Dyslipidemia			
No	62 (49.2)	18 (42.9)	44 (52.4)
Yes	64 (50.8)	24 (57.1)	40 (47.6)
Cirrhosis			
No	115 (91.3)	38 (90.5)	77 (91.7)
Yes	11 (8.7)	4 (9.5)	7 (8.3)
Chronic kidney disease			
No	91 (72.2)	33 (78.6)	58 (69.0)
Yes, not RRT^	20 (15.9)	5 (11.9)	15 (17.9)
Yes, RRT^	15 (11.9)	4 (9.5)	11 (13.1)
Chronic lung disease			
No	115 (91.3)	40 (95.2)	75 (89.3)
Yes	11 (8.7)	2 (4.8)	9 (10.7)
Cardiovascular disease			
No	106 (84.1)	37 (88.1)	69 (82.1)
Yes	20 (15.9)	5 (11.9)	15 (17.9)
Solid malignancy			
No	98 (77.8)	38 (90.5)	60 (71.4)
Yes	28 (22.2)	4 (9.5)	24 (28.6)
Hematologic malignancy			
No	105 (83.3)	33 (78.6)	72 (85.7)
Yes	21 (16.7)	9 (21.4)	12 (14.3)
HIV infection			
No	125 (99.2)	42 (100)	83 (98.8)
Yes	1 (0.8)	0 (0)	1 (1.2)
Organ transplant			
No	124 (98.4)	41 (97.6)	83 (98.8)
Yes	2 (1.6)	1 (2.4)	1 (1.2)

† Percentage by column; ‡ Percentage by row; ^RRT : Renal replacement therapy

Table 2 The prevalence of candidemia risk factors

Factors	Total n(%)†	Candidemia n(%)†	Non Candidemia n(%)†
Overall	126 (100)	42 (33.3)	84 (66.7)
ICU stay (day)			
Mean (SD)	10.9 (12.4)	9.1 (10.1)	11.9 (13.4)
Median (IQR)	8.0 (3.0-14.0)	7.0 (0-14.0)	8.5 (4.0-14.0)
Min-Max	0-74	0-36	0-74
Thoracoabdominal surgery			
No	109 (86.5)	31 (73.8)	78 (92.9)
Yes	17 (13.5)	11 (26.2)	6 (7.1)
Immunosuppressive drug			
No	103 (81.7)	35 (83.3)	68 (81.0)
Yes	23 (18.3)	7 (16.7)	16 (19.0)
Glucocorticoid			
No	96 (76.2)	30 (71.4)	66 (78.6)
Yes	30 (23.8)	12 (28.6)	18 (21.4)
Hemodialysis			
No	78 (61.9)	28 (66.7)	50 (59.5)
Yes	48 (38.1)	14 (33.3)	34 (40.5)
Prolonged use antibiotic			
No	28 (22.2)	5 (11.9)	23 (27.4)
Yes	98 (77.8)	37 (88.1)	61 (72.6)
Central catheter inserted			
No	39 (31.0)	18 (42.9)	21 (25.0)
Yes	87 (69.0)	24 (57.1)	63 (75.0)
Parenteral nutrition			
no PN	76 (60.3)	20 (47.6)	56 (66.7)
PN	50 (39.7)	22 (52.4)	28 (33.3)
Parenteral nutrition			
no PN[$]	76 (60.3)	20 (47.6)	56 (66.7)
C-PN[%]	34 (27.0)	13 (31.0)	21 (25.0)
P-PN[#]	16 (12.7)	9 (21.4)	7 (8.3)

[$] PN : Parenteral nutrition; [%] C-PN : Parenteral nutrition via central vein; [#] P-PN : Parenteral nutrition via peripheral vein

C.albican (24 of 45) and *C.glabrata* (17 of 45) were the most common candida species cultured in hemoculture, with three patients having both species.

Prolonged antibiotic use (OR 5.01, 95CI: 1.37-18.34, *p*-value = 0.015), using parenteral nutrition (OR 2.20, 95CI: 1.03-4.69, *p*-value = 0.041), and parenteral nutrition via central vascular access (OR 3.46, 95CI: 1.10-10.88, *p*-value = 0.034) were all risk factors for candidemia, but using parenteral nutrition via peripheral vascular access was not (OR 2.11, 95CI: 0.43-10.33, *p*-value = 0.358). (Table 3)

Table3 Association between risk factors and candidemia

Factors	Univariable analysis			Multivariable analysis		
	OR	95%CI	*p*-value	aOR	95%CI	*p*-value
ICU stay (day)	0.98	0.95-1.01	0.239			
Thoracoabdominal surgery						
No	1.00	Reference		1.00	Reference	
Yes	4.61	1.57-13.56	0.005	3.28	0.90-11.90	0.071
Immunosuppressive drug						
No	1.00	Reference				
Yes	0.85	0.32-2.26	0.744			
Glucocorticoid						
No	1.00	Reference				
Yes	1.47	0.63-3.43	0.376			
Hemodialysis						
No	1.00	Reference				
Yes	0.74	0.34-1.60	0.437			
Prolonged use antibiotic						
No	1.00	Reference		1.00	Reference	
Yes	2.79	0.98-7.97	0.055	5.01	1.37-18.34	0.015*
Central catheter inserted						
No	1.00	Reference		1.00	Reference	
Yes	0.44	0.2-0.98	0.043	0.53	0.16-1.74	0.296
Parenteral nutrition						
no PN[$]	1.00	Reference				
PN	2.20	1.03-4.69	0.041*			
Parenteral nutrition						
no PN[$]	1.00	Reference		1.00	Reference	
C-PN[%]	1.73	0.73-4.09	0.210	3.46	1.10-10.88	0.034*
P-PN[#]	3.60	1.18-10.94	0.024*	2.11	0.43-10.33	0.358

[$] PN : Parenteral nutrition; [%] C-PN : Parenteral nutrition via central vein; [#] P-PN : Parenteral nutrition via peripheral vein

*The factors used in multivariable analysis model considered from any factors in univariable model that *p*-value < 0.2

Parenteral nutrition administered via peripheral vascular access rather than a central venous catheter did not reduce the risk of candidemia (HR 0.88, 95CI: 0.36-2.12, *p*-value = 0.78). The type of Parenteral nutrition (HR 1.21, 95CI: 0.49-2.96, *p*-value = 0.684), the nutrition compound percentage, and the amount of total calories from parenteral nutrition did not increase candidemia risk. (Table 4)

Discussion

The patients in the study were on average 65 years old. Most patients were male (68%) and admitted to Medical ICU (85.7%). Patients in this study had a higher mortality rate (81%) than usual[1] which could be explained by the sampling method used to identify index patients, which used ICD-10 codes from discharge summaries. The coder could make an error if the patients were transferred between wards frequently and stayed for long periods of time.

Table 4 Analytic of possible candidemia risk factors

Demographic	Event	Univariable analysis		
		HR	95%CI	*p*-value
PN route access				
Central route	13	1.00	Reference	
Peripheral route	9	0.88	0.36-2.15	0.784
Type of PN				
Multi-camber bag (commercial)	10	1.21	0.49-2.96	0.684
Compounded solution	12	1.00	Reference	
Carbohydrate compound (percent)				
< 45	7	0.39	0.09-1.75	0.218
45-60	3	1.00	Reference	
> 60	12	0.42	0.11-1.56	0.196
Protein compound (percent)				
< 15	1	0.49	0.06-3.87	0.496
15-20	10	1.00	Reference	
> 20	11	0.76	0.31-1.85	0.549
Lipid compound (percent)				
<20	12	0.82	0.22-2.97	0.758
20-35	3	1.00	Reference	
>35	7	0.98	0.24-3.95	0.972
PN Calories (kcal/kg/day)				
<20	12	0.46	0.18-1.19	0.109
20-30	8	1.00	Reference	
>30	22	0.47	0.10-2.29	0.351

[$] PN : Parenteral nutrition

Prolonged use of antibiotics (OR 5.01, 95CI: 1.37-18.34, *p*-value = 0.015), using parenteral nutrition (OR 2.20, 95CI: 1.03-4.69, *p*-value = 0.041), and using parenteral nutrition via central vascular access (OR 3.46, 95CI: 1.10-10.88, *p*-value = 0.034) were all identified as risk factors for candidemia in this study, which were consistent with previous studies[5,6,7,9,10,12] that identified the inserted central catheter, using parenteral nutrition, prolonged use of antibiotics, concomitant bacteraemia and using renal replacement therapy as candidemia risk factors.

However, using parenteral nutrition via peripheral vascular access was not a risk factor (OR 2.11, 95CI: 0.43-10.33, *p*-value = 0.358) which opposed to Luzzati R, et al.'s study[11] which reported that using parenteral nutrition via peripheral vascular access increased candidemia risk. This could be explained by a study by Swindell K, et al.[9] who discovered that lipid compounds in parenteral nutrition encouraged candida to produce biofilm and grow, increasing the incidence of candidemia.

Nevertheless, at Phramongkutklao Hospital, patients' peripheral vascular access (Heparin lock) was changed every 2-3 days according to local protocols, and Swindell K et al.'s discovered that candida biofilm completely formed in media plate after 48 hours, which could explain why using parenteral nutrition via peripheral vascular access did not increase candidemia incidence in this study.

Parenteral nutrition administered via peripheral vascular access rather than a central venous catheter did not reduce the risk of candidemia (HR 0.88, 95CI: 0.36-2.12, *p*-value = 0.78). The type of parenteral nutrition (HR 1.21, 95CI: 0.49-2.96, *p*-value = 0.684), percentage of nutrition compound, and total calories from parenteral nutrition did not increase the risk of candidemia, which could be explained by the study sample size calculated for the primary objective, as well as data collection biases, which were limitations of retrospective study.

Conclusion

Candidemia were associated with prolonged use of antibiotics, using TPN, and using TPN via a central venous catheter, but not with using TPN via peripheral vascular access, as shown from the study.

Nevertheless, using the TPN via peripheral venous access over a central venous catheter did not decrease the risk of candidemia.

Moreover, changing the type of TPN, percentage of nutrition compound, or the amount of total calories from TPN did not increase candidemia risk and this may need further study.

Reference :

1. *Kullberg BJ, Arendrup MC. Invasive Candidiasis. N Engl J Med. 2015;373(15):1445-56.*
2. *Barker LA, Gout BS, Crowe TC. Hospital malnutrition: prevalence, identification and impact on patients and the healthcare system. Int J Environ Res Public Health. 2011;8(2):514-27.*
3. *Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr. 2019;38(1):48-79.*
4. *Sriram K, Meguid MM. Addition of lipids to parenteral nutrition does not cause fungal infections. Nutrition 2015;31(11-12):1443-6.*
5. *Stratman RC, Martin CA, Rapp RP, Berger R, Magnuson B. Candidemia incidence in recipients of parenteral nutrition. Nutr Clin Pract. 2010;25(3):282-9.*
6. *Tukenmez Tigen E, Bilgin H, Perk Gurun H, Dogru A, Ozben B, Cerikcioglu N, et al. Risk factors, characteristics, and outcomes of candidemia in an adult intensive care unit in Turkey. Am J Infect Control. 2017;45(6):e61-e3.*
7. *Collins CJ, Fraher MH, Bourke J, Phelan D, Lynch M. Epidemiology of catheter-related bloodstream infections in patients receiving total parenteral nutrition. Clin Infect Dis. 2009;49(11):1769-70; author reply 71-2.*
8. *Tsai CC, Lay CJ, Wang CL, Lin ML, Yang SP. Prognostic factors of candidemia among nonneutropenic adults with total parenteral nutrition. J Microbiol Immunol Infect. 2011;44(6):461-6.*
9. *Blumberg HM, Jarvis WR, Soucie JM, Edwards JE, Patterson JE, Pfaller MA, et al. Risk factors for candidal bloodstream infections in surgical intensive care unit patients: the NEMIS prospective multicenter study. The National Epidemiology of Mycosis Survey. Clin Infect Dis. 2001;33(2):177-86.*
10. *Stratov I, Gottlieb T, Bradbury R, O'Kane GM. Candidaemia in an Australian teaching hospital: relationship to central line and TPN use. J Infect. 1998;36(2):203-7.*
11. *Luzzati R, Cavinato S, Giangreco M, Granà G, Centonze S, Deiana ML, et al. Peripheral and total parenteral nutrition as the strongest risk factors for nosocomial candidemia in elderly patients: a matched case-control study. Mycoses. 2013;56(6):664-71.*
12. *Swindell K, Lattif AA, Chandra J, Mukherjee PK, Ghannoum MA. Parenteral lipid emulsion induces germination of Candida albicans and increases biofilm formation on medical catheter surfaces. J Infect Dis. 2009;200(3):473-80.*
13. *Fleiss JL, Levin B, Paik MC. Statistical methods for rates and proportions. 3rd ed. Bridgewater, NJ: John Wiley&Sons; 2003. p. 76.*