



Different evolution of *S. aureus* methicillin-resistant and methicillin-susceptible infections, Argentina

Danilo Barcudi^{a,1}, Enrique Blasko^{a,1}, María José Gonzalez^a, Paula Gagetti^b, Ricardo Lamberghini^c, Analía Garnero^d, Claudia Sarkis^e, Diego Faccone^b, Celeste Lucero^b, Dario Tosoroni^f, Study Group of *S. aureus* in Argentina^{g,2}, José L. Bocco^a, Alejandra Corso^b, Claudia Sola^{a,*}

^a Centro de Investigaciones en Bioquímica Clínica e Inmunología (CIBICI) CONICET and Universidad Nacional de Córdoba, Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Haya de La Torre y Medina Allende, Ciudad Universitaria, X5000, Córdoba, Argentina

^b Servicio Antimicrobianos, Instituto Nacional de Enfermedades Infecciosas (INEI)-ANLIS "Dr. Carlos G. Malbrán", Ciudad Autónoma de Buenos Aires, Argentina

^c Cátedra de Infectología I, Hospital Rawson, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Bajada Pucará 2025, X5000, Córdoba, Argentina

^d Servicio de Infectología, Hospital de Niños de la Santísima Trinidad de Córdoba, Córdoba, Bajada Pucará 787, X 5000, ANN, Argentina

^e Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan", Combate de los Pozos 1881, C1245, AAM, CABA, Argentina

^f Informática Médica, Facultad de Medicina, Universidad Católica de Córdoba, Jacinto Ríos 555, X5004, ASK, Córdoba, Argentina

^g ABC Hospital Español de Rosario, Rosario, Santa Fe, Argentina

ARTICLE INFO

Keywords:

S. aureus
MSSA
MRSA
Community-onset (CO) infections
Healthcare-associated (HA) infections
CA-MRSA-ST30-IV
CA-MRSA-ST5-IV
CA-MRSA-USA300-LV
CC398-MSSA
CC97-MRSA
Argentina

ABSTRACT

Staphylococcus aureus (SA) is widespread among healthcare-associated (HA) and the community-associated (CA) infections. However, the contributions of MRSA and MSSA to the SA overall burden remain unclear.

In a nationally-representative-survey conducted in Argentina, 668 SA clinical isolates from 61 hospitals were examined in a prospective, cross-sectional, multicenter study in April 2015. The study aimed to analyze MRSA molecular epidemiology, estimate overall SA infection incidence (MSSA, MRSA, and genotypes) in community-onset (CO: HACO, Healthcare-Associated-CO and CACO, Community-Associated-CO) and healthcare-onset (HO: HAHO, Healthcare-associated-HO) infections, stratified by age groups. Additionally temporal evolution was estimated by comparing this study's (2015) incidence values with a previous study (2009) in the same region. Erythromycin-resistant-MSSA and all MRSA strains were genetically typed.

The SA total-infections (TI) overall-incidence was 49.1/100,000 monthly-visits, 25.1 and 24.0 for MRSA and MSSA respectively ($P = 0.5889$), in April 2015. In adults with invasive-infections (INVI), MSSA was 15.7 and MRSA was 11.8 ($P = 0.0288$), 1.3-fold higher. HA SA infections, both MSSA and MRSA, surpassed CA infections by over threefold.

During 2009–2015, there was a significant 23.4 % increase in the SA infections overall-incidence, mainly driven by MSSA, notably a 54.2 % increase in INVI among adults, while MRSA infection rates remained stable. The MSSA rise was accompanied by increased

* Corresponding author. Centro de Investigaciones en Bioquímica Clínica e Inmunología (CIBICI) CONICET and Universidad Nacional de Córdoba, Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Haya de la Torre y M. Allende, 5000, Córdoba, Argentina.

E-mail address: csola@fcq.unc.edu.ar (C. Sola).

¹ D.B and E.B contributed equally to this work.

² Members of the Study Group are listed in the Acknowledgements section.

<https://doi.org/10.1016/j.heliyon.2023.e22610>

Received 1 August 2023; Received in revised form 14 November 2023; Accepted 15 November 2023

Available online 25 November 2023

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antimicrobial resistance, particularly to erythromycin, linked to MSSA-CC398-t1451-ermT⁺-IEC⁺-pvl emergence. The SA-infections rise was primarily attributed to community-onset-infections (37.3 % and 62.4 % increase for TI and INVI, respectively), particularly HACO-MSSA and HACO-MRSA in adults, as well as CACO-MSSA. The main CA-MRSA-PFGE-typeN-ST30-SCCmecIVc-PVL^{+/-} clone along with other clones (USA300-ST8-IV-LV-PVL^{+/-}, PFGE-typeDD-ST97-IV-PVL⁻) added to rather than replaced CA-MRSA-PFGE-typeI-ST5-SCCmecIVa-PVL^{+/-} clone in HA invasive-infections. They also displaced clone HA-MRSA-PFGE-typeA-ST5-SCCmecI, mainly in HAHO infections.

The overall-burden of SA infections is rising in Argentina, driven primarily by community-onset MSSA, particularly in adults, linked to increased erythromycin-resistance and MSSA-CC398-t1451-ermT⁺-IEC⁺-pvl emergence. Novel knowledge and transmission-control strategies are required for MSSA.

1. Introduction

Staphylococcus aureus (SA) infections, particularly methicillin-resistant SA (MRSA) pose a significant challenge to global healthcare, affecting hospitals (healthcare-associated infections/HAIs), communities (community-associated infections/CAIs), and livestock (livestock-associated infections/LAIs) [1,2]. SA causes a spectrum of human diseases, from superficial skin and soft tissue infections (SSTI) to invasive infections (INVI), sepsis, and death. This versatility arises from multiple virulence factors and differential expression abilities, primarily associated with the genotype [2,3]. The escalating concern lies in managing SA infections due to their gradual acquisition of antimicrobial resistance [4]. Notably, the associated mortality with MRSA-HAIs, in both INVI and non-INVI cases, exceeds that of most emerging multidrug-resistant gram-negative pathogens [5]. Remarkably, in 2019, SA, including both MSSA and MRSA, was globally the top bacterial cause of death [6].

Although SA is a global endemic pathogen, new strains can rapidly spread worldwide, driven by high-risk clones (HRCs) that blend increased virulence or transmission potential with multidrug resistance (MDR) [7,8]. Traditional multidrug-resistant HA-MRSA HRCs, identified in hospitals since 1959, mainly affect adult patients, with healthcare-associated risk factors (HRFs). Conversely, emerging MRSA clones (CA-MRSA) in the community since the 1980s were unrelated to healthcare. These genotypes, with diverse clonal lineages and specific geographical patterns, carry smaller SCCmec variants and fewer resistance determinants than HA-MRSA, primarily causing SSTI in healthy younger individuals [9]. Furthermore, CA-MRSA genotypes, primarily community-resident [10,11] now also cause healthcare-associated hospital-onset (HAHO) infections [9,12,13]. Therefore, genetic characterization of HRCs is essential for comprehending the evolving molecular epidemiology of SA infections in both hospital and community settings [9].

Despite MRSA HAIs decreasing in some European countries [14–16] and the United States [17–19] over the last decade, the HAHO MRSA infection rate in the US increased by 13 % in 2020 compared to 2019, attributed to the impact of COVID-19 pandemic [1]. Furthermore, in high-MRSA-prevalent regions of southern and eastern Europe, MRSA bloodstream infections (BSI) persistently rose during 2005–2018 [15], indicating ongoing challenges in effective MRSA control in highly endemic areas. Additionally, MSSA BSIs have stabilized or increased in the US [18,20] and some European countries [14,15,21,22]. Limited information exists on the global burden of SA infections from both MRSA and MSSA [15,20,21]. Despite high case fatality rates in MSSA-BSI, optimal treatment approaches remain debated [15,21]. Importantly, changes in MRSA and MSSA infection trends become evident when analyzing incidence rates, as they may be overlooked when focusing solely on the MRSA percentage among total SA infections [15].

SA is a worrying problem in hospitals of Latin America [4,9,23]. In Argentina, MRSA accounts for 40–50 % of SA isolates in both community-onset (CO) and hospital-onset (HO) infections [12,13], showing a decreasing trend [24]. Between 2002 and 2007, the HA-MRSA Cordobes/Chilean ST5-SCCmecI HRC caused over 60 % of HO-MRSA infections [25,26] while over 80 % of CA-MRSA infections were associated with the CA-MRSA pulsotypeI-ST5-SSCmecIV-PVL⁺ HRC [26,27]. Since 2009, CA-MRSA ST5-IV-PVL⁺ HRC has spread in hospitals, coinciding with declining HA-MRSA Cordobes/Chilean ST5-I HRC. Simultaneously, there has been a growing MRSA reservoir in the community linked to two main CA-MRSA HRCs: ST5-IV and ST30-IV, and minor CA-MRSA HRCs, like USA300-ST8-IV-LV (USA300 Latin American variant) [12]. Furthermore, other more recent longitudinal-multicenter study in Córdoba city (Argentina), revealed that, most imported and all hospital-acquired MRSA belonged to CA-MRSA ST30-IV and ST5-IV HRCs, with the community as the primary reservoir [13].

Importantly, there is limited awareness of the incidence evolution over time of invasive and non-invasive infections caused by MSSA and MRSA, in Latin America, and largely unknown in Argentina. The aims of this investigation were: 1) to assess the molecular epidemiology of MRSA infections and estimate overall SA infection incidence (MSSA, MRSA, and genotypes) in community-onset (CO: HACO, Healthcare-associated-CO and CACO, Community-associated-CO) and healthcare-onset (HO: HAHO, Healthcare-associated-HO) infections, stratified by age groups, 2) to evaluate the temporal evolution by comparing this study's (2015) incidence values with a previous study (2009¹²) in the same region.

2. Materials and methods

2.1. Surveillance methodology and definitions

To assess the molecular epidemiology of MRSA infections and to estimate overall SA infection incidence (MSSA, MRSA, and

Table 1
Characteristics of 341 MRSA isolates belonging to HA-MRSA and CA-MRSA genotypes, Argentina, 2015.

Genetic background	ST	PFGE type/no. (%/%) ^a	PFGE Subtype/no. (%) ^b	RIDOM <i>spa</i> type/no. (%) ^b	SCCmec no. (%) ^b	<i>pvl</i> no. (%) ^b	<i>agr</i> type	virulence genes ^c profile	Drug resistance ^d non-β-Lactam (%)
CA-MRSA n: 302									
CC30	30	N/212 (62.1/70.2)	N4/101 (47.6), N6/23 (10.8), N30/22 (10.4) N13/20 (9.4), and 26 minor subtypes.	t019: 208 (98), t021: 1, t3037: 1, t433: 1, t2529: 1	IVc: 209 (98.5), IVh: 2 (1), IVNT: 1	203 (96)	3	<i>egc-lukDE-bbp-cna</i>	GEN 24 (11.4), ERY 6 (3) ^c , CLi 3 (1.4) ^c , CLi c 3 (1.4), Cip 7 (3.3), RIF 1, MUP 1
CC5	5	1/47 (13.8/15.6)	I1/28 (59.6), I29/4 (8.5), I26/2 (4.3), I47/2 (4.3), I68/2 (4.3), and 9 minor subtypes	t311: 29 (61.7), t002: 15 (31.9), t1265: 1, t1215: 1, t062: 1	IVa: 43 (91.5), IVc: 3 (6.4), IVb: 1	32 (68.1)	2	<i>sea-egc-lukDE</i> 32 (68.1), <i>egc-lukDE</i> 15 (31.9)	GEN 5 (10.6), ERY 12 (25.5) ^c , CLi 8 (17) ^c , CLi c 3 (6.4), Cip 1
CC8	8	USA300/18 (5.3/6.0)	USA300-5/4 (22), USA300-17/2 (11), USA300-19/2 (11) and 10 minor subtypes	t008: 14 (77), t024: 2 (11), t723: 1, t068: 1	IVc: 9 (50), V ^S : 3 (16.5) IVNT ^h : 3 (16.5) IVa: 2 (11) IVb: 1	10 (56)	1	<i>pvl-lukDE-sek-seq-bsa</i> : 5 (28), <i>lukDE-bsa</i> : 3 (17), <i>lukDE-sea-bsa</i> : 3 (17), <i>pvl-lukDE-sea-sek-seq-bsa</i> : 2 (11), <i>lukDE-sea-sek-seq-bsa</i> : 1 (5), <i>pvl-lukDE-sec-sek-seq-bsa</i> : 1 (5), <i>lukDE-sec-bsa</i> : 1 (5), <i>pvl-lukDE-sed-sej-sek-seq-bsa</i> : 1 (5) <i>pvl-sed-sej-bsa</i> : 1 (5)	GEN 5 (28), ERY 4 (22.2), CLi 2 (11), CLi c 1, CIP 6 (33.3)
CC97	97	DD/12 (3.5/4.0)	DD1/5 (42), DD21/2 (17) and 4 minor subtypes	t267: 3 (25), t359: 2 (17), t1190: 2 (17), t521: 1, t8870: 1, t1247: 1, t2445: 1, t2383: 1	IVa: 10 (83), IVc: 2 (17)	0 (0)	1	<i>lukDE</i> 12 (100)	GEN 3 (25), ERY 1, CLi 1
CC8	72	R/10 (2.9/3.3)	R1/6 (60) and 4 minor subtypes	t148: 10 (100)	IVc: 9 (90), IVa: 1	0 (0)	1	<i>egc-lukDE</i> 10 (100)	GEN 4 (40), ERY 1 (10), CLi 1 (10), CIP 2 (20), RIF 2 (20) TMS 1
CC509	207	Y/2 (0.6/0.7)	Y1/1 (50), Y4 1 (50)	t525	IVa: 2 (100)	0 (0)	3	<i>egc^f-etaa</i> -1 (50), <i>egc^f-cna</i> 1 (50)	
CC6	1649	QQ/1 (0.1/0.3)	QQ2	t701	IVNT ^h	0 (0)	1	<i>lukDE-seb-sea-bsa-cna</i>	TMS
HA-MRSA n: 39									
CC5	5	A/24 (7.0/61.5)	A102/3 (12.5), A10/2 (8.3), A40/2 (8.3), and 15 minor subtypes	t149 22 (92), t15913: 1, t17035: 1	I: 24 (100)	0 (0)	2	<i>egc-lukDE</i>	GEN 21 (88), ERY 24 (100), CLi c 24 (100), CIP 23 (96), TMS 1, RIF 1
CC5	100	C/15 (4.4/38.5)	C30/6 (40), and 9 minor subtypes	t002: 9 (60), t045: 2 (13) t1084, t1791, t548	NT 11 (73) IVNv: 4 (27)	0 (0)	2	<i>egc-lukDE</i>	GEN 14 (93), ERY 8 (53), CLi c 6 (40), CLi 2 (13), CIP 9 (60), RIF 13 (87) MIN 1

CC, Clonal Complex; ST, Sequence Type, PFGE type/subtype, Pulsed Field Gel Electrophoresis type and subtypes; RIDOM *spa* type: staphylococcal protein A (*spa*) type assigned through the RIDOM databases (<http://spaserver.ridom.de>); The *spa* type was used to predict sequence types (STs). MLST was carried out in at least one strain of each *spa*-type detected, <https://pubmlst.org/organisms/staphylococcus-aureus> database, SCCmec: Type of Staphylococcal Cassette Chromosome *mec* (SCCmec NT: it was not possible to ascertain a class of *mec* complex or a type of *ccr*); *pvl*, Pantone Valentine leukocidin genes (*lukS*-PV-*lukF*-PV); *agr* type, type of accessory gene regulator allotype.

^a no. (%/%), number and % of total MRSA (n: 668)/% of each genotype [CA-MRSA_G (n: 302) or HA-MRSA_G (n: 39)].

^b no. (%), number and % of strains with this molecular characteristic [PFGE subtype (only those more frequent are indicated) or *spa* type or SCCmec type or *pvl* genes] belonging to each genetic background: CA-MRSA_G (n: 302) or HA-MRSA_G (n: 39) genotypes. % is not expressed when only one isolate with this characteristic was detected.

^c Virulence genes profile: The enterotoxins: *sea*, *seb*, *sec*, *sed*, *see*, *seg*, *seh*, *sei*, *sej*, *sen*, *seo*, *sem*, *seq* and *sek*; toxic shock syndrome toxin 1 (TSST-1): *ts*; exfoliative toxins: *eta* and *etb*; leukocidin: *lukE-lukD* and the class F leukocidin: *lukM*; bacteriocine (*bsa*), adhesins: for collagen (*cna*) and for bone

sialoprotein-binding protein (*bbp*) and the *arcA* gene (indicator of the arginine catabolic mobile element, ACME) were analyzed and those detected are indicated (number and % of positive isolates is expressed when not all isolates harbor this virulence factor).

^d Drug resistance to non- β -Lactams (%), is indicated as follows: Gentamicin (GEN), Erythromycin (ERY), Clindamycin (CLiC and CLiI: constitutive and inducible resistance to macrolide, lincosamide and streptogramin B, respectively), Ciprofloxacin (CIP), Rifampin (RIF), Trimethoprim/Sulfamethoxazole (SXT), Minocycline (MIN) and Mupirocin (MUP), (%) of strains resistant to these antibiotics within each genetic background is indicated when more than one isolate was detected.

^e $P < 0.01$ by χ^2 test, for comparison between MRSA isolates characterized as pulsotype N and those with pulsotype I for resistance to clindamycin and erythromycin antibiotics.

^f The *egc* locus appears to be present in a variant or truncated form with only genes *sem*, *sei* and *seo* being detectable.

^g SCCmec Vv: positive for *ccrC* locus and class C2 *mec* gene complex and negative for J1 region of SCCmec V and for other SCCmec regions analyzed.

^h IV NT: SCCmec type IV non typable.

genotypes: CA-MRSA_G, HA-MRSA_G and principal MRSA clones) in community-onset (HACO and CACO) and healthcare-onset (HAHO) infections, we conducted a prospective-observational cross-sectional multicenter study in Argentina in April 2015. Sixty-one hospitals, including 46 from the WHONET Argentina Network, participated in this study across 20 provinces and Buenos Aires City (CABA). The hospitals characteristics are shown in the [Supplementary Table S1](#). Additionally, a longitudinal-retrospective study was conducted to estimate the overall temporal evolution of SA infection incidence and prevalence (including MSSA, MRSA and genotypes) by comparing this study's (2015) values with a previous study (2009 [12]). In the prior study, 591 clinical isolates were recovered from 66 hospitals serving a population of 1,484,505 visits, including 961,424 adults and 523,081 pediatric cases, in November 2009. Briefly, in both studies the patients were prospectively and consecutively identified according to the results of SA clinical cultures, as reported by the microbiology laboratories. Only the first isolate from each patient was evaluated. A standardized questionnaire was completed for each patient and for this study the following features were analyzed: *i*) demographic characteristics (age and sex, [Supplementary Table S2](#)), *ii*) HRFs, CDC criteria [12,28] *iii*) onset of infection (hospital vs. community), *iv*) characteristics and severity of infections ([Supplementary Table S2](#)). Invasive infections (INVI) were defined as previously described [12]. Surgical site infections (SSI) were not considered as skin diseases.

We genetically characterized each MRSA clone and, to facilitate comparison between the two studies, we additionally defined traditional CA-MRSA and HA-MRSA strain types genotypically (detailed below), referred to as CA-MRSA_G and HA-MRSA_G ([Table 1](#)). Regardless of the strain types involved, cases were classified by infection onset [healthcare-onset (HO) and community-onset (CO)] and healthcare risk factors (HRFs) presence/absence [following epidemiological definitions: Community-associated CO-infections (CACO) and Healthcare-associated (HA) infections, including both HO-infections (HAHO) and CO-infections (HACO) [28]], as described previously [12].

From administrative data provided by each hospital, we determined the total number of patients served in each hospital (stratified by age groups) in both studies (2009 and 2015) across the northern, central, and southern regions of Argentina. We calculated the incidence of SA, MSSA, MRSA, and genotypes (CA-MRSA_G, HA-MRSA_G, and major clones) infections per 100,000 visits in each period (cases/100,000 monthly visits, including admissions, outpatient facilities, and emergency services). Aggregated data from all hospitals were used to calculate overall incidence rates and compare both periods. The analysis considered all infection cases, stratified by age groups (<19 and \geq 19 years, representing pediatric and adult patients, respectively), infection categories (HO [HOHA] and CO [CACO, HACO]), and regions of Argentina (North, Center, and South) [12], [Tables 2–5](#) and [Supplementary Tables S3 and S4](#).

2.2. Ethics statement

This study was reviewed and approved by the Ethics Review Board of Health Research for adults and children (CIEIS), Government of the Province of Córdoba, Health Ministry (approval No. 2531, 2551 and 2552/2015) as well as by the institutional Ethical Review Board of each Hospital listed in acknowledgments. All participants/patients (or their proxies/legal guardians) provided informed consent to participate in the study.

2.3. Bacterial isolates and antimicrobial susceptibility

SA clinical isolates (n: 668) were identified by standard microbiologic procedures and antimicrobial susceptibility testing was performed by disk diffusion method and/or Vitek2 [29]. Vancomycin minimum inhibitory concentrations (MICs), were determined by agar dilution method [29]. Mupirocin susceptibility was determined by E-test method (bioMérieux) with the following definitions: high-level resistance, MIC \geq 512 μ g/mL; low-level resistance, MIC = 8–64 μ g/mL; susceptible, MIC \leq 4 μ g/mL [30]. High-level resistance to mupirocin was confirmed by detection of the *mupA* gene by PCR as described [31]. To genetically investigate the rising incidence of erythromycin-resistant MSSA detected in the longitudinal study, all such isolates from both periods underwent molecular typing and PCR analysis for erythromycin resistance determinants (*ermA*, *ermB*, *ermC*, *ermT*, and *msrA1* genes) [32].

2.4. Molecular typing

In all MRSA isolates and in erythromycin-resistant MSSA isolates from this study (n: 46) and the previous one (n:20), PFGE of *Sma*I digests of chromosomal DNA and *spa* typing were performed and interpreted as previously described [12]. The *spa*-types were assigned using the RIDOM web server (<http://spaserver.ridom.de/>). Additionally, the *spa* server was employed to predict sequence types (STs),

Table 2

Percentage and incidence of total (TI) and invasive (INVI) infections caused by *S. aureus* (SA), including MSSA, MRSA and MRSA-genotypes in Argentine hospitals by age group: 2009 vs. 2015, with comparisons in 2015 between pediatric vs. adult patients and MRSA vs. MSSA for TI and INVI.

		<i>S. aureus</i> infections									
		% (n)/incidence of total cases and % (INV)/incidence of invasive cases									
		Total			Adults (≥19)			Pediatrics (<19)			
		2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	Pediatric vs.
		N ^a : 591 INV ^b :296	N ^a : 668	P value/OR (95% CI)	N ^a : 366	N ^a : 417 INV ^b :	P value/OR (95% CI)	N ^a : 225	N ^a : 251 INV ^b :	P value/OR (95%CI)	Adults
		%(n)/In ^c /% (INV)/InI ^d	INV ^b :363		INV ^b :188	242		INV ^b : 108	121		2015
			%(n)/In ^c /% (INV)/InI ^d		%(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d		%(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d		P value/OR (95% CI)
SA		100 (591)	100 (668)		100 (366)	100 (417)		100 (225)	100 (251)		
Total		39.8	49.1	0.002/1.2 (1.10–1.38)	38.1	47.4	0.0022/1.2 (1.08–1.43)	43.0	52.3	0.033/1.2 (1.02–1.46)	0.2155
SA		100 (296)	100 (363)		100 (188)	100 (242)		100 (108)	100 (121)		
INV		19.9	26.1	0.0002/1.3 (1.15–1.56)	19.6	27.5	0.0004/1.4 (1.16–1.70)	20.6	25.2	0.14	0.44
MSSA		45.5 (269)	49.0 (327)	0.22	46.7 (171)	53.7 (224)	0.07	43.6 (98)	41.0 (103)	0.63	0.0015/0.60 (0.44–0.82)
Total		18.1	24.0	0.0006/1.3 (1.13–1.56)	17.8	25.4	0.0004/1.4 (1.17–1.75)	18.7	21.4	0.33	0.15
MSSA		48.3 (143)	55.4 (201)	0.08	50.5 (95)	57.0 (138)	0.21	44.4 (48)	52.1 (63)	0.30	0.44
INV		9.6	14.8	0.0001/1.5 (1.24–1.90)	9.9	15.7	0.0005/1.6 (1.22–2.06)	9.2	13.1	0.06	0.24
MRSA		54.5 (322)	51.0 (341)	0.23	53.3 (195)	46.3 (193)	0.07	56.4 (127)	59.0 (148)	0.56	0.0015/1.7 (1.22–2.29)
Total		21.7	25.1	0.06	20.3	21.9	0.44	24.3	30.8	0.047/1.3 (1.00–1.61)	0.0017/1.4 (1.14–1.74)
MRSA		51.7 (153)	44.6 (162)	0.42	49.5 (93)	43.0 (104)	0.21	55.5 (60)	47.9 (58)	0.30	0.44
INV		10.3	11.9	0.45	9.7	11.8	0.17	11.5	12.1	0.82	0.89
In MSSA vs.		0.0292/0.84	0.59		0.21	0.13		0.06	0.0045/0.70		
MRSA		(0.71–0.98)							(0.54–0.89)		
P value/OR											
(95%CI)											
InI MSSA vs.		0.5610	0.041/1.2		0.8840	0.028/1.3		0.2482	0.6494		
MRSA			(1.01–1.53)			(1.03–1.71)					
P value/OR											
(95%CI)											
CA-MRSA_G		38.7 (229)	45.2 (302)	<0.0001/1.7	31.1 (114)	38.8 (162)	0.0210/1.4	51.1 (115)	55.8 (140)	0.33	<0.0001/2.0
Total		15.4	22.2	(1.32–2.06)	11.9	18.4	(1.04–1.89)	21.9	29.2	0.024/1.3	(1.45–2.73)
				(1.21–1.71)			(1.22–1.97)			(1.04–1.70)	(1.26–2.00)
CA-MRSA_G		26.4 (78)	35.8 (130)	0.009/1.6	16.0 (30)	32.2 (78)	0.0001/2.5	44.4 (48)	43.0 (52)	0.93	0.06
INV		5.2	9.6	(1.12–2.18)	3.1	8.9	(1.56–4.01)	9.2	10.8	0.42	0.26
				<0.0001/1.8			(1.87–4.31)				
				(1.37–2.41)			<0.0001/2.8				
HA-MRSA_G		15.7 (93)	5.8 (39)	<0.0001/0.3	22.1 (81)	7.4 (31)	<0.0001/0.3	5.3 (12)	3.2 (8)	0.44	0.0234/0.41
Total		6.2	2.9	(0.22–0.49)	8.4	3.5	(0.18–0.44)	2.3	1.7	0.48	(0.19–0.89)
				<0.0001/0.5			<0.0001/0.4				0.06
				(0.32–0.66)			(0.28–0.63)				

(continued on next page)

Table 2 (continued)

	S. aureus infections									
	% (n)/incidence of total cases and % (INV)/incidence of invasive cases									
	Total			Adults (≥19)			Pediatrics (<19)			
	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	Pediatric vs.
	N ^a : 591 INV ^b :296	N ^a : 668	P value/OR (95% CI)	N ^a : 366	N ^a : 417 INV ^b : 242	P value/OR (95% CI)	N ^a : 225	N ^a : 251 INV ^b : 121	P value/OR (95%CI)	Adults 2015
	%(n)/In ^c /% (INV)/InI ^d	INV ^b :363 %(n)/In ^c /% (INV)/InI ^d		INV ^b :188 %(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d		INV ^b : 108 %(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d		P value/OR (95% CI)
HA-MRSA _G	25.3 (75)	8.8 (32)	0.0001/0.3 (0.18–0.44)	33.5 (63)	10.7 (26)	<0.0001/0.2 (0.14–0.40)	11.1 (12)	5.0 (6)	0.14	0.10
INV	5.1	2.4	0.0002/0.5 (0.31–0.70)	6.6	3.0	0.0001/0.4 (0.26–0.65)	2.3	1.3	0.21	0.06
N-ST30-IV ^e	17.6 (104)	31.7 (212)	<0.0001/2.2 (1.67–2.84)	17.5 (64)	25.7 (107)	0.0057/1.6 (1.15–2.30)	17.8 (40)	41.8 (105)	<0.0001/3.3 (2.2–5.1)	<0.0001/2.1 (1.49–2.91)
Total	7.0	15.6	<0.0001/2.2 (1.76–2.81)	6.6	12.1	<0.0001/1.8 (1.34–2.49)	7.6	21.9	<0.0001/2.9 (1.9–4.1)	<0.0001/1.8 (1.38–2.35)
N-ST30-IV ^e	7.8 (23)	21.2 (77)	<0.0001/3.2 (2.25–5.48)	5.3 (10)	17.8 (43)	0.0001/3.9 (1.9–7.77)	12.0 (13)	28.1 (34)	0.0027/2.8 (1.43–5.71)	0.0232/1.8 (1.08–3.02)
INV	1.5	5.7	<0.0001/3.7 (2.30–5.80)	1.0	4.9	<0.0001/4.7 (2.39–9.21)	2.5	7.1	0.0008/2.9 (1.52–5.35)	0.10
I-ST5-IV ^e	17.2 (102)	7.0 (47)	<0.0001/0.4 (0.25–0.52)	10.7 (39)	5.8 (24)	0.0119/0.5 (0.30–0.87)	28.0 (63)	9.2 (23)	<0.0001/0.3 (0.2–0.4)	0.13
Total	6.9	3.4	0.0001/0.5 (0.36–0.71)	4.1	2.7	0.12	12.0	4.8	0.0001/0.4 (0.3–0.6)	0.06
I-ST5-IV ^e	14.2 (42)	6.9 (25)	0.0020/0.4 (0.27–0.75)	7.4 (14)	6.2 (15)	0.76	25.9 (28)	8.3 (10)	0.0003/0.3 (0.12–0.55)	0.46
INV	2.8	1.8	0.08	1.5	1.7	0.84	5.4	2.1	0.0079/0.4 (0.19–0.79)	0.62
A-ST5-I ^e	10.3 (61)	3.6 (24)	<0.0001/0.3 (0.20–0.52)	15.8 (58)	4.8 (20)	<0.0001/0.3 (0.16–0.47)	1.3 (3)	1.6 (4)	0.91	0.06
Total	4.1	1.8	0.0003/0.4 (0.27–0.69)	6.0	2.3	0.0001/0.4 (0.23–0.62)	0.6	0.83	0.62	0.06
A-ST5-I ^e	15.9 (47)	5.2 (19)	<0.0001/0.3 (0.17–0.51)	23.4 (44)	6.6 (16)	<0.0001/0.2 (0.13–0.42)	2.8 (3)	2.5 (3)	0.78	0.10
INV	3.2	1.4	0.0020/0.4 (0.26–0.75)	4.6	1.8	0.0113/0.4 (0.23–0.70)	0.6	0.6	0.92	0.08
C-ST100-IVNv ^e ,	3.6 (21)	2.2 (15)	0.18	3.6 (13)	2.6 (11)	0.18	3.6 (8)	1.6 (4)	0.27	0.56
Total	1.4	1.1	0.46	1.3	1.2	0.84	1.5	0.8	0.39	0.48
C-ST100-IVNv ^e , INV	5.7 (17)	3.6 (13)	0.09	4.8 (9)	4.1 (10)	0.90	7.4 (8)	2.5 (3)	0.15	0.63
	1.1	0.96	0.58	0.9	1.1	0.85	1.5	0.6	0.17	0.41
USA300-ST8-IV ^e	0.8 (5)	2.7 (18)	0.0145/3.3 (1.24–8.46)	1.1 (4)	2.9 (12)	0.08	0.4 (1)	2.4 (6)	0.13	0.71
Total	0.3	1.3	0.0035/3.9 (1.52–10.18)	0.4	1.4	0.0294/3.3 (1.12–9.62)	0.2	1.2	0.06	0.86
USA300-ST8-IV ^e	1.0 (3)	1.3 (9)	0.12	1.6 (3)	2.9 (7)	0.38	0 (0)	1.7 (2)	NA	0.47
INV	0.2	0.7	0.06	0.3	0.8	0.16	0	0.4	NA	0.41
DD-ST97-IV ^e	0.7 (4)	1.8 (12)	0.08	0.8 (3)	1.7 (7)	0.29	0.4 (1)	2.0 (5)	0.13	0.77
Total										

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Table 2 (continued)

S. aureus infections % (n)/incidence of total cases and % (INV)/incidence of invasive cases										
Total			Adults (≥19)			Pediatrics (<19)			Pediatric vs. Adults	
2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	2015	
N ^a : 591 INV ^b :296	N ^a : 668	P value/OR (95% CI)	N ^a : 366	N ^a : 417 INV ^b : 242	P value/OR (95% CI)	N ^a : 225	N ^a : 251 INV ^b : 121	P value/OR (95%CI)	P value/OR (95% CI)	
%(n)/In ^c /% (INV)/InI ^d	INV ^b :363		INV ^b :188	242		INV ^b : 108	121			
	%(n)/In ^c /% (INV)/InI ^d		%(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d		%(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d			
	0.3	0.9	0.0295/3.3 (1.11–9.62)	0.3	0.8	0.16	0.2	1.0	0.11	0.76
DD-ST97-IV^c	1.0 (3)	1.5 (10)	0.08	1.1 (2)	2.1 (5)	0.42	0.9 (1)	4.1 (5)	0.21	0.31
INV	0.2	0.7	0.035/3.6 (1.10–12.20)	0.2	0.6	0.21	0.2	1.0	0.11	0.51

CA-MRSA_G and HA-MRSA_G community-associated and healthcare-associated methicillin-resistant *S. aureus* genotypes.

% (n) of cases and % (n) of INV isolates, NA: Not applicable.

^a N: Total number of patients with *S. aureus* infections in each category (total, adults, pediatrics).

^b INV: Total number of patients with *S. aureus* invasive infections in each category (total, adults, pediatrics).

^c In: Incidence: Number of cases/100.000 monthly visits. Number of visits (V): include outpatient facility, emergency service and admissions during that month.

^d InI: Invasive infections incidence: Number of cases of invasive infections/100.000 monthly visits. Number of visits (V): include outpatient facility, emergency service and admissions during that month.

^e Genotypes (major clones) are denoted as: type (by PFGE)-Sequence Type (ST by MLST)-SCCmec type P values ≤ 0.05 for all comparisons are shown in boldface font.

Table 3

Percentage and incidence of total (TI) and invasive (INVI) infections caused by *S. aureus* (SA), including MSSA, MRSA and MRSA-genotypes in Argentine hospitals, by onset type and epidemiological criteria: 2009 vs. 2015, with comparisons in 2015 between infection types and MRSA vs. MSSA for TI and INVI.

		<i>S. aureus</i> infections															
		% (n)/incidence of total cases and % (INV)/incidence of invasive cases															
		Hospital onset (HO) (HAHO)			Community onset (CO) (CACO + HACO)			2015		Community-associated-community-onset (CACO)			Healthcare-associated community-onset (HACO)			2015	
		2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	CO vs. HAHO	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	HACO vs. CACO	HACO vs. HAHO	
		N ^a : 216	N ^a : 197	P value/OR	N ^a : 375	N ^a : 471	P value/OR	P value/OR	N ^a : 222	N ^a : 253	P value/OR	N ^a : 153	N ^a : 218	P value/OR	P value/OR	P value/OR	
		INV ^b :158	INV ^b :158	(95%CI)	INV ^b :138	INV ^b : 205	P value/OR	(95%CI)	INV ^b :58	INV ^b : 79	P value/OR	INV ^b :80	INV ^b : 126	(95%CI)	(95%CI)	(95%CI)	
		%(n)/In ^c	%(n)/In ^c		%(n)/In ^c %	%(n)/In ^c			%(n)/In ^c %	INV ^b : %		%(n)/In ^c %	INV ^b : %				
		% (INV)/InI ^d	% (INV)/InI ^d		(INV)/InI ^d	% (INV)/InI ^d			(INV)/InI ^d	% (INV)/InI ^d		(INV)/InI ^d	% (INV)/InI ^d				
SA	Total	100 (216)	100 (197)		100 (375)	100 (471)			100 (222)	100 (253)		100 (153)	100 (218)				
		14.6	14.5	0.54	25.2	34.6	<0.0001/1.4 (1.21–1.63)	<0.0001/2.4 (2.03–2.82)	15.0	18.6	0.0175/1.2 (1.04–1.49)	10.3	16.0	<0.0001/1.6 (1.27–1.91)	0.10	0.30	
SA	INV	100 (158)	100 (158)		100 (138)	100 (205)			100 (58)	100 (79)		100 (80)	100 (126)				
		10.6	11.6	0.77	9.3	15.1	<0.0001/1.6 (1.31–2.01)	0.0136/1.3 (1.05–1.60)	3.9	5.8	0.0210/1.5 (1.06–2.08)	5.4	9.2	<0.0001/1.7 (1.30–2.27)	0.0010/1.6 (1.59–1.20)	0.06	
MSSA	Total	50.9 (110)	48.2 (95)	0.65	42.4 (159)	49.3 (232)	0.053	0.86	38.7 (86)	45.8 (116)	0.14	47.7 (73)	53.2 (116)	0.35	0.13	0.31	
		7.5	7.0	0.41	10.7	17.1	<0.0001/1.6 (1.31–1.98)	<0.0001/2.4 (1.92–3.10)	5.8	8.5	0.0063/1.5 (1.11–1.94)	4.9	8.5	0.0002/1.7 (1.30–2.32)	0.99	0.15	
MSSA	INV	48.7 (77)	51.2 (82)	0.57	47.8 (66)	58.0 (119)	0.062	0.24	41.4 (24)	59.5 (47)	0.0360/2.1 (1.05–4.12)	52.5 (42)	57.1 (72)	0.57	0.73	0.46	
		5.2	6.0	0.54	4.4	8.7	<0.0001/1.9 (1.46–2.66)	0.0091/1.5 (1.10–1.92)	1.6	3.5	0.0019/2.1 (1.31–3.48)	2.8	5.3	<0.0010/1.9 (1.28–2.73)	0.0201/1.53 (1.06–2.21)	0.42	
MRSA	Total	49.1 (106)	51.8 (102)	0.65	57.6 (216)	50.8 (239)	0.053	0.8075	61.3 (136)	54.2 (137)	0.11	52.3 (80)	46.8 (102)	0.35	0.13	0.31	
		7.1	7.5	0.96	14.6	17.6	0.044/1.2 (1.01–1.45)	<0.0001/2.3 (1.86–2.95)	9.2	10.1	0.43	5.4	7.5	0.0263/1.4 (1.04–1.86)	0.0236/0.7 (0.58–0.96)	>0.99	
MRSA	INV	51.3 (81)	48.1 (76)	0.57	52.2 (72)	42.0 (86)	0.062	0.24	58.6 (34)	40.5 (32)	0.0360/0.5 (0.24–0.95)	47.5 (38)	42.9 (54)	0.57	0.73	0.46	
		5.5	5.6	0.54	4.9	6.3	0.09	0.43	2.3	2.4	0.98	2.6	3.9	0.0367/1.6 (1.03–2.34)	0.0177/1.70 (1.09–2.61)	0.06	
In: MSSA vs. MRSA		0.79	0.62		0.0032/0.74 (0.60–0.90)	0.75			0.0008/0.6 (0.48–0.83)	0.19		0.57	0.34				

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Table 3 (continued)

		<i>S. aureus</i> infections % (n)/incidence of total cases and % (INV)/incidence of invasive cases														
		Hospital onset (HO) (HAHO)			Community onset (CO) (CACO + HACO)			2015	Community-associated-community-onset (CACO)			Healthcare-associated community-onset (HACO)			2015	
		2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	CO vs. HAHO	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	HACO vs. CACO	HACO vs. HAHO
		N ^a : 216	N ^a : 197	P value/OR	N ^a : 375	N ^a : 471	P value/OR	P value/OR	N ^a : 222	N ^a : 253	P value/OR	N ^a : 153	N ^a : 218	P value/OR	P value/OR	P value/OR
		INV ^b :158	INV ^b :158	(95%CI)	INV ^b :138	INV ^b : 205	P value/OR	(95%CI)	INV ^b :58	253	P value/OR	INV ^b :80	218	(95%CI)	P value/OR	P value/OR
		%(n)/In ^c	%(n)/In ^c		%(n)/In ^c /%	%(n)/In ^c			%(n)/In ^c /%	INV ^b :	(95%CI)	%(n)/In ^c /%	INV ^b :		(95%CI)	(95%CI)
		% (INV)/In ^d	% (INV)/In ^d		(INV)/In ^d	% (INV)/In ^d			(INV)/In ^d	79		In ^c /%	126			
										%(n)/In ^c		In ^c	%(n)/In ^c			
										In ^c		In ^d	In ^c			
										%			%			
										(INV)/In ^d			(INV)/In ^d			
										In ^d			In ^d			
	(95% CI)															
	InI: MSSA vs. MRSA	0.75	0.63		0.61	0.021/1.38			0.19	0.09		0.65	0.11			
	P value/OR (95% CI)					(1.05–1.82)										
CA-MRSA _G	Total	15.7 (34)	38.6 (76)	<0.0001/3.4 (2.1–5.3)	52.0 (195)	48.0 (226)	0.27	0.026/1.5	60.8 (135)	53.8 (136)	0.14	39.2 (60)	41.3 (90)	0.77	0.007/0.6	0.57
	INV	2.3	5.6	<0.0001/2.4 (1.63–3.65)	13.1	16.6	0.0161/1.3	<0.0001/3.0	9.1	10.0	0.43	4.0	6.6	0.0028/1.6	(1.18–2.27)	0.0022/0.7
CA-MRSA _G	INV	14.5 (23)	34.2 (54)	<0.0001/2.3 (1.8–5.3)	39.8 (55)	37.1 (76)	0.60	0.56	58.6 (34)	39.2 (31)	0.0248/0.5	26.3 (21)	35.7 (45)	0.15	0.61	0.79
	INV	1.5	3.9	0.0001/2.6	3.7	5.6	0.0194/1.5	0.054	2.3	2.3	0.98	1.4	3.3	0.0009/2.3	(1.40–3.91)	0.11
HA-MRSA _G	Total	33.3 (72)	13.2 (26)	<0.0001/0.3 (0.2–0.5)	5.6 (21)	2.8 (13)	0.06	<0.0001/0.19	0.5 (1)	0.4 (1)	0.59	13.1 (20)	5.5 (12)	0.0174/0.4	0.0007/14.68	0.0067/0.4/
	INV	4.9	1.9	<0.0001/0.4 (0.25–0.61)	1.4	1.0	0.26	0.037/0.50	0.1	0.07	0.95	1.3	0.9	0.25	0.0023/12.0	0.0231/ (2.21–65.27)
HA-MRSA _G	INV	36.7 (58)	13.9 (22)	<0.0001/0.3 (0.2–0.5)	12.3 (17)	4.5 (10)	0.0121/0.4	0.002/0.3	0 (0)	1.2 (1)	NA	21.3 (17)	7.1 (9)	0.0030/0.3	0.06	0.07
	INV	3.9	1.6	0.0001/0.4	1.1	0.7	0.26	0.033/0.50	0	0.07	NA	1.1	0.7	0.17	0.0114/9.0	.0165/0.4
N-ST30-IV ^e	Total	1.9 (4)	20.3 (40)	<0.0001/13.5 (4.9–36.5)	26.7 (100)	33.5 (172)	0.0023/1.6	<0.0001/2.3	36.5 (81)	42.3 (107)	0.23	11.8 (18)	29.8 (65)	<0.0001/3.2 (1.81–5.61)	0.0005/0.6	0.0260/1.7
	INV	0.3	2.9	<0.0001/10.9 (4.12–28.90)	6.7	12.6	<0.0001/1.9	<0.0001/4.3	5.5	7.9	0.0125/1.4	1.2	4.8	<0.0001/3.9 (2.35–6.60)	0.0014/0.61	0.0147/1.6

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Table 3 (continued)

S. aureus infections % (n)/incidence of total cases and % (INV)/incidence of invasive cases															
	Hospital onset (HO) (HAHO)			Community onset (CO) (CACO + HACO)			2015	Community-associated-community-onset (CACO)			Healthcare-associated community-onset (HACO)			2015	
	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	CO vs. HAHO	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	HACO vs. CACO	HACO vs. HAHO
	N ^a : 216	N ^a : 197	P value/OR	N ^a : 375	N ^a : 471	P value/OR	P value/OR	N ^a : 222	N ^a : 253	P value/OR	N ^a : 153	N ^a : 218	P value/OR	P value/OR	P value/OR
	INV ^b :158	INV ^b :158	(95%CI)	INV ^b :138	INV ^b : 205	P value/OR	(95%CI)	INV ^b :58	253	P value/OR	INV ^b :80	218	(95%CI)	P value/OR	P value/OR
	%(n)/In ^c	%(n)/In ^c		%(n)/In ^c /%	%(n)/In ^c	(95%CI)		%(n)/In ^c /%	INV ^b :		%(n)/In ^c /%	INV ^b :		(95%CI)	(95%CI)
	% (INV)/In ^d	% (INV)/In ^d		(INV)/In ^d	% (INV)/In ^d			(INV)/In ^d	79		(INV)/In ^d	126			
									%			%			
									(INV)/In ^d			(INV)/In ^d			
N-ST30-IV^e	1.3 (2)	13.3 (21)	<0.0001/12.0	15.2 (21)	27.3 (56)	0.0084/2.1	0.0012/2.5	27.6 (16)	32.9	0.50	6.3 (5)	23.8	0.00811/4.7	0.09	0.0218/2.0
INV			(3.2–45.2)			(1.2–3.6)	(1.42–4.24)	(26)	(26)		(30)	(30)	(1.80–12.20)		(1.11–3.75)
	0.1	1.5	<0.0001/11.9	1.4	4.1	<0.0001/2.9	0.0001/2.7	1.1	1.9	0.06	0.3	2.2	<0.0001/6.6	0.59	0.21
			(3.09–42.5)			(1.77–4.78)	(1.62–4.38)						(2.64–16.24)		
I-ST5-IV^e	9.7 (21)	8.6 (17)	0.38	21.6 (81)	6.4 (30)	<0.0001/0.25	0.40	21.6 (48)	6.3	<0.0001/0.2	22.2	6.4	<0.0001/0.24	0.88	0.51
Total						(0.2–0.4)		(16)	(16)	(0.14–0.44)	(34)	(14)	(0.12–0.46)		
	1.4	1.2	0.58	5.5	2.2	<0.0001/0.4	0.06	3.2	1.2	0.0003/0.4	2.3	1.0	0.0097/0.45	0.71	0.59
						(0.3–0.6)				(0.21–0.64)			(0.24–0.83)		
I-ST5-IV^c	9.5 (15)	9.5 (15)	>0.99	19.6 (27)	4.9 (10)	<0.0001/0.2	0.085	25.9 (15)	2.5 (2)	<0.0001/0.07	15.0	6.3 (8)	0.0410/0.38	0.21	0.33
INV						(0.1–0.5)				(0.02–0.30)	(12)	(8)	(0.15–0.96)		
	1.0	1.1	0.92	1.8	0.7	0.0114/0.4	0.31	1.0	0.15	<0.0029/0.15	0.8	0.6	0.48	0.06	0.14
						(0.20–0.82)				(0.04–0.55)					
A-ST5-I^c	23.6 (51)	9.1 (18)	<0.0001/0.3	2.7 (10)	1.3 (6)	0.22	<0.0001/0.13	0 (0)	0 (0)	NA	6.5 (10)	2.8 (6)	0.14	NA	0.0054/0.3
Total			(0.2–0.5)				(0.05–0.32)								(0.11–0.70)
	3.4	1.3	0.0003/0.4	0.67	0.44	0.44	0.0143/0.33	0	0	NA	0.7	0.4	0.41	NA	0.0143/0.3
			(0.23–0.66)				(0.14–0.81)								(0.14–0.81)
A-ST5-I^c	25.3 (40)	9.5 (15)	0.0002/0.3	5.0 (7)	1.9 (4)	0.11	0.0014/0.19	0 (0)	0 (0)	NA	8.8 (7)	3.2 (4)	0.08	NA	0.0342/0.3
INV			(0.2–0.6)				(0.06–0.55)								(0.11–0.92)
	2.7	1.1	0.0023/0.23	0.5	0.3	0.39	0.0116/0.3	0	0	NA	0.5	0.3	0.44	NA	0.0116/0.3
			(0.23–0.73)				(0.09–0.76)								(0.09–0.76)
C-ST100-IVNv^e	6.0 (13)	4.0 (8)	0.48	2.1 (8)	1.5 (7)	0.15	0.08	0.5 (1)	0.4 (1)	0.59	4.6 (7)	2.8 (6)	0.52	0.08	0.69
Total															
	0.9	0.6	0.30	0.5	0.5	0.92	0.81	0.1	0.07	0.95	0.5	0.4	0.90	0.06	0.59
C-ST100-IVNv^e	6.3 (10)	4.4 (7)	0.45	5.0 (7)	2.9 (6)	0.31	0.44	0 (0)	1.2 (1)	NA	8.8 (7)	3.9 (5)	0.15	0.26	0.69
INV															
	0.7	0.5	0.50	0.5	0.4	0.85	0.78	0	0.07	NA	0.5	0.4	0.67	0.1	0.56

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Table 4

Percentage and incidence of total (TI) and invasive (INVI) infections caused by *S. aureus* (SA), including MSSA, MRSA and MRSA-genotypes in Argentine hospitals, by age group, onset type and epidemiological criteria: 2009 vs. 2015, with comparisons in 2015 between infection types, pediatric vs. adult patients and MRSA vs. MSSA for TI and INVI.

S. aureus infections in pediatric (<19) and adult (≥19) patients															
% (n)/incidence of general cases and % (INV)/incidence of invasive cases															
	Community onset (CO) (CACO + HACO)						Hospital onset (HO) (HAHO)						2015		
	Adults			Pediatrics			Adults			Pediatrics			Adults	Pediatrics	
	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	Adults	Pediatrics	
	N ^a : 215/ INV ^b :75	N ^a : 301/ INV ^b :141	P value/OR (95%CI)	N ^a : 160/ INV ^b : 63	N ^a : 170/ INV ^b : 64	P value/OR (95%CI)	Adults P value/OR (95%CI)	N ^a : 151/ INV ^b :113	N ^a : 116/ INV ^b :101	P value/OR (95%CI)	N ^a : 65/ INV ^b :45	N ^a : 81/ INV ^b :57	P value/OR (95%CI)	P value/OR (95%CI)	
	%(n)/ In ^c /% (INV)/ InI ^d	%(n)/In ^c /% (INV)/InI ^d		%(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d			%(n)/ In ^c /% (INV)/ InI ^d	%(n)/ In ^c /% (INV)/ InI ^d		%(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d			
SA	100	100 (301)		100 (160)	100 (170)			100	100		100 (65)	100 (81)			
Total	22.4	34.2	<0.0001/1.5 (1.28–1.82)	30.6	35.4	0.18	0.72	15.7	13.2	0.15	12.4	16.9	0.07	0.08	
														<0.0001/2.6 (2.10–3.20)	
														2.1 (1.61–2.73)	
SA	100 (75)	100 (141)		100 (63)	100 (64)			100	100		100 (45)	100 (57)			
INV	7.8	16.0	<0.0001/2.1 (1.55–2.72)	12.0	13.3	0.56	0.22	11.8	11.5	0.86	8.6	11.9	0.10	0.83	
														0.0101/1.4 (1.08–1.80)	
														0.53	
MSSA	45.6	55.1 (166)	0.0321/1.5 (1.03–2.09)	38.1 (61)	38.8 (66)	0.97	0.0007/ 0.52 (0.35–0.76)	48.3 (73)	50.0 (58)	0.86	56.9 (37)	45.7 (37)	0.23	0.65	
Total	10.2	18.8	<0.0001/1.9 (1.44–2.37)	11.7	13.8	0.35	0.0293/ 0.73 (0.55–0.97)	7.6	6.6	0.18	7.1	7.7	0.73	0.51	
														<0.0001/2.9 (2.12–3.86)	
														0.0043/1.9 (1.20–2.66)	
MSSA	56.0	61.0 (86)	0.57	38.1 (24)	51.6 (33)	0.17	0.27	46.9 (53)	51.5 (52)	0.59	53.3 (24)	52.6 (30)	0.89	0.89	
INV	4.4	9.8	<0.0001/2.2 (1.55–3.23)	4.6	6.9	0.45	0.08	5.5	5.9	0.62	4.6	6.2	0.25	0.0038/1.7 (1.17–2.33)	
														0.71	
MRSA	54.4	44.9 (135)	0.0321/0.68 (0.48–0.97)	61.9 (99)	61.2 (104)	0.97	0.0007/1.9 (1.32–2.84)	51.7 (78)	50.0 (58)	0.86	43.1 (28)	54.3 (44)	0.23	0.66	
Total	12.2	15.3	0.07	18.9	21.7	0.33	0.0078/1.4 (1.09–1.82)	8.1	6.6	0.22	5.4	9.2	0.0243/1.7 (1.07–2.74)	0.09	
														<0.0001/2.3 (1.71–3.16)	
														2.4 (1.66–3.36)	
MRSA	44.0	39.0 (55)	0.57	61.9 (39)	48.4 (31)	0.17	0.27	53.1 (60)	48.5 (49)	0.59	46.7 (21)	47.4 (27)	0.88	0.89	
INV	3.4	6.2	0.0058/1.8 (1.19–2.80)	7.4	6.5	0.45	0.88	6.2	5.6	0.56	6.2	5.2	0.24	0.81	
														0.56	
														0.60	
In: MSSA vs.	0.1950	0.07		0.0027/0.62 (0.45–0.85)	0.0036/ 0.63 (0.47–0.86)			0.68	0.99		0.26	0.44			
MRSA															
P															
value/ OR (95% CI)															

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Table 4 (continued)

		S. aureus infections in pediatric (<19) and adult (≥19) patients % (n)/incidence of general cases and % (INV)/incidence of invasive cases														
InI: MSSA vs. MRSA	0.2988	0.009/1.60 (1.12–2.19)		0.06	0.80			0.51	0.77		0.65	0.69				
<i>p</i> value/ OR (95% CI)																
CA-MRSA_G Total	47.0 (101)	40.9(123)	0.19	58.8 (94)	60.6 (103)	0.79	<0.0001/2.2 (1.52–3.26)	8.6 (13)	33.6 (39)	<0.0001/5.4 (2.7–10.6)	32.3 (21)	45.7 (37)	0.13	0.09	0.21	0.0262/1.8 (1.07–3.11)
	10.5	13.9	0.0312/1.3 (1.02–1.73)	17.9	21.5	0.21	0.0012/1.5 (1.18–1.99)	1.4	4.4	0.0001/3.3 (1.77–6.08)	4.0	7.7	0.0151/1.9 (1.13–3.26)	0.0145/1.7 (1.11–2.72)	<0.0001/3.2 (2.20–4.51)	<0.0001/2.9 (1.92–4.05)
CA-MRSA_G INV	28.0 (21)	31.9 (45)	0.66	54.0 (34)	48.4 (31)	0.65	0.0232/2.0 (1.10–3.65)	8.0 (9)	32.7 (33)	<0.0001/5.6 (2.56–12.26)	31.1 (14)	36.8 (21)	0.69	0.56	0.94	0.27
	2.2	5.1	0.0009/2.3 (1.40–3.91)	6.5	6.5	0.99	0.31	0.9	3.7	<0.0001/4.0 (1.95–8.23)	2.7	4.4	0.15	0.56	0.17	0.17
HA-MRSA_G Total	7.4 (16)	4.0 (12)	0.19	3.1 (5)	0.6 (1)	0.21	0.0306/ 0.14 (0.03–0.78)	43.0 (65)	16.4 (19)	<0.0001/0.3 (0.14–0.46)	10.8 (7)	8.6 (7)	0.84	0.11	<0.0001/0.2 (0.10–0.45)	0.0009/0.1 (0.01–0.32)
	1.7	1.4	0.66	1.0	0.2	0.26	0.0421/ 0.15 (0.03–0.81)	6.8	2.2	<0.0001/0.3 (0.19–0.53)	1.3	1.5	0.88	0.37	0.21	0.0339/0.1 (0.02–0.82)
HA-MRSA_G INV	16.0 (12)	7.1 (10)	0.07	7.9 (5)	0 (0)	NA	NA	45.1 (51)	15.8 (16)	<0.0001/0.2 (0.12–0.44)	15.6 (7)	10.5 (6)	0.69	0.35	0.06	NA
	1.2	1.1	0.85	1.0	0	NA	NA	5.3	1.8	0.0001/0.3 (0.20–0.60)	1.3	1.3	0.99	0.43	0.24	NA
N-ST30-IV^e Total	27.9 (60)	30.6 (92)	0.51	25.0 (40)	47.1 (80)	<0.0001/2.7 (1.67–4.25)	0.0004/2.0 (1.37–2.97)	2.6 (4)	12.9 (15)	0.0012/5.5 (1.9–16.1)	0 (0)	30.9 (25)	NA	0.0007/3.3 (1.63–6.70)	0.0002/3.0 (1.65–5.34)	0.0150/2.0 (1.14–3.47)
	6.2	10.4	<0.0017/1.7 (1.21–2.32)	7.6	16.7	<0.0001/2.2 (1.49–3.18)	0.0021/1.6 (0.47–0.85)	0.4	1.7	0.0066/4.1 (1.43–11.70)	0 (0)	5.2	NA	0.0003/3.1 (1.63–5.75)	<0.0001/6.1 (3.58–10.50)	<0.0001/3.2 (2.05–5.00)
N-ST30-IV^e INV	10.7 (8)	23.4 (33)	0.023/2.6 (1.14–5.76)	20.6 (13)	35.9 (23)	0.086	0.09	1.8 (2)	9.9 (10)	0.0145/6.1 (1.49–24.90)	0 (0)	19.3 (11)	NA	0.09	0.0067/2.8 (1.32–5.87)	0.0679
	0.83	3.7	<0.0001/4.5 (2.12–9.56)	2.5	4.8	0.054	0.36	0.2	1.1	0.0137/5.5 (1.37–21.69)	0 (0)	2.3	NA	0.10	0.0005/3.3 (1.65–6.60)	0.0396/2.1 (1.03–4.23)
I-ST5-IV^e Total	14.4 (31)	5.0 (15)	0.0002/0.3 (0.16–0.59)	31.3 (50)	8.8 (15)	<0.0001/0.2 (0.11–0.40)	0.15	5.3 (8)	7.8 (9)	0.56	20.0 (13)	9.9 (8)	0.083	0.79	0.39	0.98
	3.2	1.7	0.0321/0.53 (0.29–0.97)	9.6	3.1	0.0001/0.3 (0.19–0.58)	0.09	0.8	1.0	0.85	2.5	1.7	0.36	0.31	0.22	0.14
I-ST5-IV^e INV	10.7 (8)	4.3 (6)	0.12	30.2 (19)	6.3 (4)	0.0005/0.2 (0.05–0.46)	0.79	5.3 (6)	8.9 (9)	0.44	20.0 (9)	10.5 (6)	0.28	0.92	0.23	0.61
	0.83	0.7	0.71	3.6	0.8	0.0035/0.23 (0.08–0.64)	0.85	0.6	1.0	0.34	1.7	1.3	0.35	0.70	0.45	0.52
A-ST5-I^e Total	4.7 (10)	2.0 (6)	0.12	0 (0)	0 (0)	NA	NA	31.8 (48)	12.1 (14)	<0.0001/0.09 (0.04–0.17)	2.8 (3)	2 (4)	0.95	0.14	<0.0001/0.2 (0.06–0.38)	NA

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Table 4 (continued)

S. aureus infections in pediatric (<19) and adult (≥19) patients																
% (n)/incidence of general cases and % (INV)/incidence of invasive cases																
	1.0	0.7	0.42	0	0		NA	5.0	1.6	<0.0001/0.3 (0.18–0.57)	0.6	0.8	0.62	0.32	0.08	NA
A-ST5-I^c	9.3 (7)	2.8 (4)	0.08	0 (0)	0 (0)		NA	32.7 (37)	11.9 (12)	0.0004/0.29 (0.14–0.58)	6.7 (3)	5.3 (3)	0.89	0.26	0.0177/0.3 (0.09–0.81)	NA
INV	0.7	0.5	0.44	0	0		NA	3.8	1.4	0.0011/0.3 (0.19–0.67)	0.6	0.6	0.99	0.21	0.0455/0.3 (0.11–0.98)	NA
C-ST100- IVNv^e	2.8 (6)	2.0 (6)	0.23	2.5 (4)	0.6 (1)	0.20	0.45	6.0 (9)	4.3 (5)	0.54	6.2 (4)	3.7 (3)	0.49	0.87	0.33	0.19
Total	0.6	0.5	0.62	0.7	0.2	0.37	0.21	0.9	0.6	0.35	0.7	0.6	0.78	0.71	0.74	0.31
C-ST100- IVNv^e	4.0 (3)	4.3 (6)	0.88	6.3 (4)	0 (0)	NA	NA	5.3 (6)	4.0 (4)	0.89	8.9 (4)	5.3 (3)	0.74	0.89	0.89	NA
INV	0.3	0.7	0.25	0.8	0	NA	NA	0.6	0.5	0.85	0.8	0.6	0.79	0.86	0.53	NA
Healthcare-associated-community-onset (HACO)																
Community-associated-community-onset (CACO)																
	Adult			Pediatric			2015	Adult			Pediatric			2015	Adult	Pediatric
	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	Pediatric vs. 2009	2009	2015	2015 vs. 2009	2009	2015	2015 vs. 2009	Pediatric vs. 2009	HACO vs. CACO	HACO vs. CACO
	N ^a : 93/ INV ^b :46	N ^a : 147/ INV ^b :94	P value/OR (95%CI)	N ^a : 60/ INV ^b :34	N ^a : 71/ INV ^b :32	P value/OR (95%CI)	Adults P value/OR (95%CI)	N ^a : 122/ INV ^b :29	N ^a : 154 INV ^b : 47	P value/OR (95%CI)	N ^a : 100/ INV ^b :29	N ^a : 99 INV ^b : 32	P value/OR (95%CI)	Adults P value/OR (95%CI)	CACO P value/OR (95%CI)	CACO P value/OR (95%CI)
	%(n)/ In ^c /% (INV)/ InI ^d	%(n)/In ^c /% (INV)/InI ^d		%(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/InI ^d			%(n)/ In ^c /% (INV)/ InI ^d	%(n)/ In ^c /% (INV)/ InI ^d		%(n)/In ^c /% (INV)/InI ^d	%(n)/In ^c /% (INV)/ InI ^d		%(n)/In ^c /% (INV)/ InI ^d	% (INV)/ InI ^d	
SA	100	100 (147)		100 (60)	100 (71)			100	100		100 (100)	100 (99)				
Total	(93)							(122)	(154)							
	9.7	16.7	<0.0001/1.7 (1.33–2.24)	11.5	14.8	0.15	0.40	12.7	17.5	0.0078/1.4 (1.09–1.75)	19.2	20.6	0.5920	0.20	0.69	0.0317/ 0.7/ (0.53–0.97)
SA	100	100 (94)		100 (34)	100 (32)			100 (29)	100 (47)		100 (29)	100 (32)				
INV	(46)															
	4.8	10.7	<0.0001/2.2 (1.57–3.17)	6.5	6.7	0.92	0.0011/0.6 (0.42–0.93)	3.0	5.3	0.0142/1.8 (1.12–2.80)	5.5	6.7	0.4712	0.33	0.0001/2.0 (1.41–2.83)	>0.99
MSSA	47.3	58.5 (86)	0.12	48.3 (29)	42.3 (30)	0.49	0.0242/0.5 (0.29–0.92)	44.3 (54)	51.9 (80)	0.26	32.0 (32)	36.4 (36)	0.6137	0.0152/ 0.53 (0.32–0.88)	0.30	0.43
Total	(44)															
	4.6	9.8	<0.0001/1.5 (1.49–3.06)	5.5	6.3	0.65	0.0337/0.6 (0.42–0.97)	5.6	9.1	0.0058/1.6 (1.15–2.28)	6.1	7.5	0.05561	0.39	0.64	0.46
MSSA	50.0	59.6 (56)	0.37	55.9 (19)	50.0 (16)	0.63	0.34	65.5 (19)	63.8 (30)	0.92	17.3 (5)	53.1 (17)	0.0036/5.44 (1.72–17.18)	0.34	0.77	0.80
INV	(23)															
	2.4	6.4	<0.0001/2.7 (1.64–4.30)	3.6	3.3	0.56	0.0204/0.5 (0.30–0.91)	2.0	3.4	0.06	1.0	3.5	0.0057/3.7 (1.42–9.66)	0.89	0.0051/1.9 (1.20–2.90)	0.86

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Table 4 (continued)

S. aureus infections in pediatric (<19) and adult (≥19) patients % (n)/incidence of general cases and % (INV)/incidence of invasive cases																
MRSA Total	52.7 (49)	41.5 (61)	0.12	51.7 (31)	57.7 (41)	0.49	0.0242/1.9 (1.09–3.41)	55.7 (68)	48.1 (74)	0.26	68.0 (68)	63.6 (63)	0.6137	0.0152/1.9 (1.13–3.17)	0.30	0.43
	5.1	6.9	0.11	5.9	8.5	0.12	0.29	7.1	8.4	0.30	13.0	13.1	0.9561	0.0088/1.6 (1.12–2.18)	0.26	0.0310/0.7 (0.44–0.96)
MRSA INV	50.0 (23)	40.4 (38)	0.37	44.1 (15)	50.0 (16)	0.63	0.34	34.5 (10)	36.2 (17)	0.956	82.7 (24)	46.9 (15)	0.036/0.18 (0.06–0.58)	0.34	0.7650	0.80
	2.4	4.3	0.0234/1.8 (1.08–3.01)	2.9	3.3	0.66	0.38	1.0	1.9	0.11	4.6	3.1	0.2404	0.17	0.0046/2.2 (1.27–3.93)	0.86
In: MSSA vs MRSA P value/ OR (95%CI)	0.6041	0.039/1.40 (1.02–1.96)		0.79	0.19			0.21	0.63		0.0003/0.47 (0.31–0.71)	0.0067/0.57 (0.38–0.86)				
In: MSSA vs MRSA P value/ OR (95%CI)	0.9999	0.063		0.49	0.99			0.09	0.06		0.0004/0.21 (0.08–0.53)	0.72				
CA-MRSA_G Total	36.6 (34)	34.0 (50)	0.79	43.3 (26)	56.3 (40)	0.14	0.0017/2.5 (1.41–4.45)	54.9 (67)	47.4 (73)	0.63	68.0 (68)	63.6 (63)	0.6137	0.0115/1.9 (1.16–3.25)	0.0182/0.6 (0.36–0.91)	0.34
	3.5	5.7	0.0314/1.6 (1.04–2.48)	4.0	8.3	0.0380/1.7 (1.03–2.74)	0.07	7.0	8.3	0.31	13.0	13.1	5.0	0.0082/1.6 (1.13–2.21)	0.0381/0.7 (0.48–0.98)	0.0234/0.6 (0.43–0.94)
CA-MRSA_G INV	23.9 (11)	30.9 (29)	0.51	29.4 (10)	50.0 (16)	0.09	0.06	34.5 (10)	34.0 (16)	0.97	82.7 (24)	46.9 (15)	0.036/0.18 (0.06–0.58)	0.25	0.86	0.80
	1.1	3.3	0.0018/2.9 (1.46–5.69)	1.9	3.3	0.16	0.96	1.0	1.8	0.16	4.6	3.1	0.2404	0.0011/2.8 (1.47–5.14)	0.05	0.86
HA-MRSA_G Total	16.1 (15)	7.5 (11)	0.06	8.3 (5)	1.4 (1)	0.09	0.12	0.9 (1)	0.6 (1)	0.67	0 (0)	0 (0)		NA	0.0025/12.4 (2.22–68.91)	NA
	1.6	1.2	0.57	1.0	0.2	0.13	0.24	0.1	0.1	0.99	0.0	0.0		NA	0.0039/11.0 (2.01–60.30)	NA
HA-MRSA_G INV	26.1 (12)	9.6 (9)	0.0206/0.3 (1.12–0.76)	14.7 (5)	0 (0)	NA	NA	0 (0)	2.1 (1)	NA	0 (0)	0 (0)		NA	0.20	NA
	1.3	1.0	0.66	1.0	0.0	NA	NA	0.0	0.1	NA	0.0	0.0		NA	0.0114/9.0 (1.61–50.36)	NA
N-ST30-IV^E Total	12.9 (12)	23.1 (34)	0.07	10 (6)	43.7 (31)	< 0.0001/6.9 (2.73–17.81)	0.0019/2.6 (1.41–4.70)	39.3 (48)	37.7 (58)	0.88	34.0 (34)	49.5 (49)	0.0267/1.9 (1.08–3.36)	0.09	0.0062/0.5 (0.30–0.82)	0.45
	1.2	3.8	0.0004/3.1 (1.62–5.91)	1.1	6.5	0.0004/5.6 (2.42–13.10)	0.0363/1.7 (1.03–2.71)	5.0	6.6	0.15	6.5	10.2	0.0410/1.6 (1.02–2.4)	0.0022/1.6 (1.06–2.26)	0.0123/0.6 (0.38–0.89)	0.0442/0.6 (0.40–0.99)
N-ST30-IV^E INV	6.5 (3)	20.2 (19)	0.0366/3.6 (1.10–12.02)	5.9 (7)	34.4 (11)	0.0036/8.4 (1.92–35.53)	0.10	17.2 (5)	29.8 (14)	0.33	37.9 (11)	37.5 (12)	0.9897	0.45	0.29	0.79
	0.3	2.2	0.0003/6.9 (2.22–21.58)	0.4	2.3	0.0080/5.9 (1.53–23.54)	0.88	0.5	1.6		0.02342/3.06 (1.15–8.16)	2.1	2.5	0.9561	0.25	0.38

(continued on next page)

Table 4 (continued)

S. aureus infections in pediatric (<19) and adult (≥19) patients																
% (n)/incidence of general cases and % (INV)/incidence of invasive cases																
I-ST5-IV ^c	16.1	4.8 (7)	0.0029/0.26	30.0 (18)	9.9 (7)	0.0035/0.26	0.26	13.1 (16)	5.2 (8)	0.0204/0.36	32.0 (32)	8.1 (8)	< 0.0001/	0.57	0.91	0.69
Total	(15)		(0.10–0.65)			(0.10–0.65)				(0.15–0.86)			0.19			
	1.7	0.8	0.13	3.4	1.5	0.0469/0.4	0.25	1.7	0.9	0.15	6.1	1.7	0.0004/0.27	0.23	0.79	0.79
						(0.18–0.99)							(0.13–0.58)			
I-ST5-IV ^c	10.9 (5)	5.3 (5)	0.39	20.6 (7)	9.4 (3)	0.20	0.41	10.3 (3)	2.1 (1)	0.30	41.4 (12)	3.1 (1)	0.0003/0.05	0.78	0.66	0.81
INV													(0.01–0.27)			
	0.5	0.6	0.85	1.4	0.6	0.26	0.87	0.3	0.1	0.36	2.3	0.2	0.0037/0.09	0.86	0.10	0.31
													(0.02–0.49)			
A-ST5-I ^e	10.7	4.1 (6)	0.08	0 (0)	0 (0)			0 (0)	0 (0)		0 (0)	0 (0)			NA	
Total	(10)															
	1.0	0.7	0.41	0.0	0.0			0.0	0.0		0.0	0.0			NA	
A-ST5-I ^e	15.2 (7)	4.2 (4)	0.05	0 (0)	0 (0)			0 (0)	0 (0)		0 (0)	0 (0)			NA	
INV																
	0.7	0.5	0.59	0.0	0.0			0.0	0.0		0.0	0.0			NA	
C-ST100-	3.2 (3)	3.4 (5)	0.78	6.7 (4)	1.4 (1)	0.50	0.69	0.8 (1)	0.6 (1)	0.60	1.4 (1)	0 (0)		NA	0.18	NA
IVNv^e																
	0.3	0.6	0.41	0.8	0.2	0.21	0.34	1.0	0.1	0.99	0.0	0.0		NA	0.10	NA
Total																
C-ST100-	6.5 (3)	5.3 (5)	0.99	11.7 (4)	0 (0)	NA	NA	0 (0)	2.1 (1)	NA	0 (0)	0 (0)		NA	0.66	NA
IVNv^e																
	0.3	0.6	0.41	0.8	0	NA	NA	0.0	0.1	NA	0.0	0.0		NA	0.10	NA
INV																

CA-MRSA_G and HA-MRSA_G community-associated and healthcare-associated methicillin-resistant *S. aureus* genotypes.

% (n) of cases and % (n) of INV isolates, NA: Not applicable.

^a N: Total number of pediatric patients with *S. aureus* infections in each category [healthcare onset (HO or HAHO), community onset (CO: including CACO + HACO), community-associated community-onset infections (CACO), healthcare-associated community-onset (HACO)].

^b INV: Total number of patients with invasive *S. aureus* infections in each category.

^c In: Incidence: Number of cases/100,000 monthly visits. Number of visits (V) include: outpatient facility, emergency service and admissions during that month.

^d InI: Incidence of Invasive infections: Number of cases of invasive infections/100,000 monthly visits. Number of visits (V) include: outpatient facility, emergency service and admissions during that month.

^e Genotypes (major clones) are denoted as: type (by PFGE)-Sequence Type (ST by MLST)-SCCmec type. *P* values ≤ 0.05 for all comparisons are shown in boldface font.

Table 5

Staphylococcus aureus (SA) infections across hospitals from Argentine provinces and Buenos Aires city (2015): percentage and incidence by region, including MSSA, MRSA and MRSA genotypes; comparisons with 2009 data.

	<i>S. aureus</i> infections % (n)/incidence of cases of infections											
	North			Centre			South			2015		
	2009 N ^a : 86 %(n)/In ^b	2015 N ^a : 144 %(n)/In ^b	2009 vs. 2015 P value/OR (95%CI)	2009 N ^a : 433 %(n)/ In ^b	2015 N ^a : 446 %(n)/ In ^b	2009 vs. 2015 P value/OR (95%CI)	2009 N ^a : 72 %(n)/In ^b	2015 N ^a : 78 %(n)/In ^b	2009 vs. 2015 P value/OR (95%CI)	North vs Centre P value/OR (95%CI)	North vs South P value/OR (95%CI)	Centre vs South P value/OR (95%CI)
SA	100 (86)	100 (144)		100 (433)	100 (446)		100 (72)	100 (78)				
	76.5	81.1	0.68	34.7	41.0	0.0128/1.2 (1.04–1.35)	58.0	81.4	0.0370/1.4 (1.02–1.93)	<0.0001/2.0 (1.64–2.39)	0.98	<0.0001/0.50 (0.40–0.64)
MSSA	18.6 (16)	27.1 (39)	0.21	46.7 (202)	51.6 (230)	0.19	70.8 (51)	74.4 (58)	0.78	<0.0001/0.35 (0.23–0.53)	<0.0001/0.13 (0.07–0.24)	0.0002/0.37 (0.21–0.63)
	14.2	21.9	0.14	16.2	21.2	0.0053/1.3 (1.08–1.58)	41.1	60.5	0.041/1.5 (1.01–2.14)	0.82	<0.0001/0.36 (0.24–0.54)	<0.0001/0.35 (0.26–0.47)
MRSA	81.4 (70)	72.9 (105)	0.21	53.3 (231)	48.4 (216)	0.19	29.2 (21)	25.6 (20)	0.78	<0.0001/2.9 (1.90–4.32)	<0.0001/7.9 (4.19–14.54)	0.0002/2.7 (1.59–4.66)
	62.2	59.1	0.73	18.5	19.9	0.45	16.9	20.8	0.50	<0.0001/3.0 (2.36–3.76)	<0.0001/2.8 (1.77–4.55)	0.83
In: MSSA vs MRSA P value/ OR (95% CI)	<0.0001/0.23 (0.13–0.39)	<0.0001/0.37 (0.26–0.54)		0.1634	0.5073		0.0004/2.4 (1.47–4.02)	<0.0001/2.9 (1.75–4.80)				
CA-MRSA_G	72.1 (62)	65.9 (95)	0.42	36.0 (156)	43.0 (192)	0.0330/1.3 (1.02–1.76)	15.3 (11)	19.2 (15)	0.67	<0.0001/2.6 (1.73–3.79)	<0.0001/8.1 (4.24–15.64)	0.0001/3.1 (1.77–5.70)
	55.1	53.5	0.85	12.5	17.7	0.0130/1.4 (1.14–1.75)	8.9	15.6	0.14	<0.0001/3.0 (2.37–3.87)	<0.0001/3.4 (2.00–5.85)	0.65
HA-MRSA_G	9.3 (8)	6.9 (10)	0.51	17.3 (75)	5.4 (24)	<0.0001/0.3 (0.17–0.44)	13.9 (10)	6.4 (5)	0.20	0.48	0.88	0.71
	7.1	5.6	0.62	6.0	2.2	<0.0001/0.4 (0.23–0.58)	8.1	5.2	0.42	0.0099/2.6 (1.24–5.26)	0.88	0.07

(continued on next page)

Table 5 (continued)

	S. aureus infections % (n)/incidence of cases of infections											
	North			Centre			South			2015		
	2009 N ^a : 86 %(n)/In ^b	2015 N ^a : 144 %(n)/In ^b	2009 vs. 2015 P value/OR (95%CI)	2009 N ^a : 433 %(n)/ In ^b	2015 N ^a : 446 %(n)/ In ^b	2009 vs. 2015 P value/OR (95%CI)	2009 N ^a : 72 %(n)/In ^b	2015 N ^a : 78 %(n)/In ^b	2009 vs. 2015 P value/OR (95%CI)	North vs Centre P value/OR (95%CI)	North vs South P value/OR (95%CI)	Centre vs South P value/OR (95%CI)
N-ST30-IV^c	54.7 (47)	44.4 (64)	0.13	12.5 (54)	31.4 (140)	<0.0001/3.2 (2.27–4.54)	2.8 (2)	10.3 (8)	0.07	0.0042/2.0 (1.19–2.57)	<0.0001/7.0 (3.20–15.32)	<0.0001/4.0 (1.91–8.38)
	41.8	36.0	0.43	4.3	12.9	<0.0001/2.4 (1.57–3.61)	1.6	8.3	0.0211/5.2 (1.26–21.22)	<0.0001/2.8 (2.08–3.76)	<0.0001/4.3 (2.11–8.83)	0.22
I-ST5-IV^c	16.3 (14)	9.7 (14)	0.14	18.9 (82)	6.7 (30)	<0.0001/0.3 (0.20–0.48)	11.1 (8)	3.8 (3)	0.09	0.2341	0.11	0.33
	12.5	7.9	0.22	6.6	2.8	<0.0001/0.4 (0.28–0.64)	6.4	3.1	0.27	0.0007/2.8 (1.53–5.34)	0.13	0.83
A-ST5-I^c	8.1 (7)	4.9 (7)	0.31	10.8 (47)	2.7 (12)	<0.0001/0.2 (0.12–0.438)	9.7 (7)	6.4 (5)	0.45	0.1996	0.62	0.08
	6.2	3.9	0.38	3.8	1.1	<0.0001/0.3 (016–0.55)	5.6.	5.2	0.89	0.0040/3.6 (1.44–8.83)	0.63	0.0013/0.21 (0.08–0.58)
C-ST100- IVNv^c	0 (0)	2.1 (3)	NA	1.8 (8)	2.7 (12)	0.40	4.2 (3)	0 (0)	NA	0.6873	NA	NA
	0.0	1.7	NA	0.6	1.1	0.40	2.4	0.0	NA	0.7104	NA	NA
USA300-ST8- IV^c	0 (0)	5.6 (8)	NA	1.2 (5)	1.6 (7)	0.82	0 (0)	3.8 (3)	NA	0.0138/3.7 (1.36–10.03)	0.5753	0.1752
	0.0	4.5	NA	0.4	0.6	0.41	0.0	3.1	NA	<0.0001/7.0 (2.62–18.68)	0.5885	0.0414/0.21 (0.06–0.73)
DD-ST97-IV^c	0 (0)	3.5 (5)	NA	0.7 (3)	1.6 (7)	0.35	0 (0)	0 (0)	0.1596	0.1596	NA	NA
	0.0	2.8	NA	0.2	0.6	0.20	0.0	0	<0.0059/4.4 (1.45–13.14)	<0.0059/4.4 (1.45–13.14)	NA	NA

CA-MRSA_G and HA-MRSA_G community-associated and healthcare-associated methicillin-resistant *S. aureus* genotypes.

V₂₀₀₉: North: 112,427; Centre: 1,247,957 and South 124,121 visits.

V₂₀₁₅: North: 177,554; Centre: 1,086,859 and South 95,839 visits. NA: Not applicable.

^a N: Total number of patients with *S. aureus* infections in each Argentina region.

^b In: Incidence: Number of cases/100,000 monthly visits. Number of visits (V): include outpatient facility, emergency service and admissions during that month.

^c Genotypes (major clones) are denoted as: type (by PFGE)-Sequence Type (ST by MLST)-SCC_{mec} type.

as previously described [13]. Briefly, when the STs could not be determined using the *spa* server, Multi-locus-sequence-typing (MLST) was performed. Thus, MLST was carried out in at least one strain of each *spa*-type detected. Allele numbers, sequence types (STs), and clonal complexes (CCs) were assigned using the <https://pubmlst.org/organisms/staphylococcus-aureus> database.

All MRSA isolates were screened by PCR for accessory gene regulator (*agr*) type, for 24 specific staphylococcal virulence genes (detailed in Table 1), including Panton-Valentine leukocidin genes (*lukS*-PV-*lukF*-PV), *sasX* and for *arcA* gene (indicator of the arginine catabolic mobile element, (CME), as described elsewhere [12]. All CC398-MSSA isolates (n: 10) were screened by PCR [32] for immune evasion cluster (IEC) genes (*scn*, *chp*, *sak*, *sea*, and *sep*) to determine the potential animal or human origin of our isolates, as well as for *lukS*-PV-*lukF*-PV genes [12].

The *SCCmec* types (including the new variant of *SCCmec* IV/IVNv associated to ST100 in Argentina) were evaluated for all MRSA isolates by multiplex PCR and by allotyping (to identify *mec*, *ccr*, and the J1 region of I-XIV *SCCmec* types) by conventional PCR as described [12,33].

The genotypic definition for the identification of CA-MRSA_G and HA-MRSA_G was used as previously described [12]. Briefly, CA-MRSA_G were defined as belonging to the following genotypes: ST5-IV-t311 and related, PVL^{+/-}, ST30-IV-t019 and related, PVL^{+/-}, ST72-IV-t148 and related, PVL⁻, ST8-IV-t008, PVL^{+/-}, ST97-IV-t267 and related, PVL⁻, ST207-IV-t525, PVL⁻, ST1649 (SLV of ST6)-IV-t701, PVL⁻ [12]. All remaining genotypes were considered HA-MRSA_G [9,12].

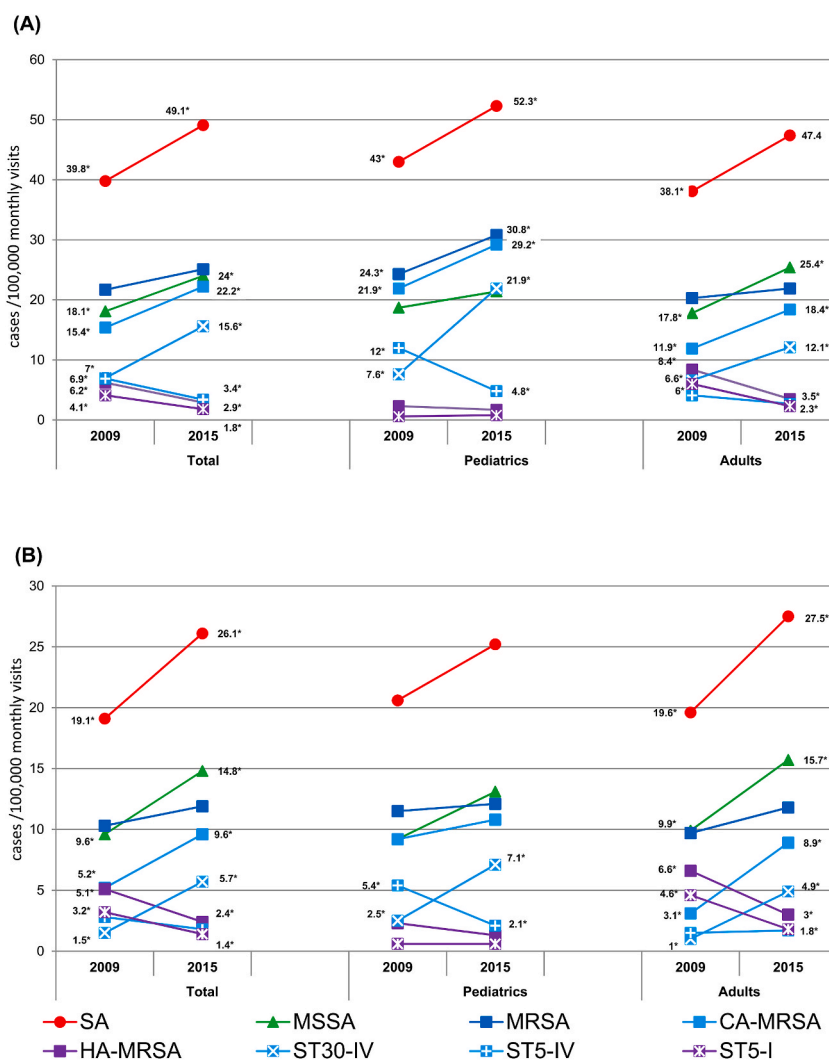


Fig. 1. Incidence of cases of (A) total and (B) invasive infections caused by *S. aureus* (SA), MSSA, MRSA and MRSA genotypes (including CA-MRSA_G and HA-MRSA_G and major MRSA clones) in the total population and by age group, 2009 and 2015, Argentina. Abbreviation: n*: $P < 0.05$ by χ^2 test for the comparison between 2009 and 2015 of infections incidence.

Incidence: Number of cases/100,000 monthly visits. Number of visits (V): include outpatient facility, emergency service and admissions during one month.

2.5. Statistical analysis

Comparisons between groups were performed with χ^2 test or Fisher's exact test, as appropriate and $P < 0.05$ was considered statistically significant. Data were analyzed using SPSS (version 15.0) and InfoStat (www.infostat.com.ar).

3. Results

3.1. Prospective observational cross-sectional multicenter study (2015)

a) Characteristics of SA infections cases

The population served by all hospitals (Supplementary Table S1) consisted of 1,360,252 visits, with 880,279 (64.5 %) visits from adults and 479,973 (35.3 %) visits from pediatric patients with 45,809 admissions during one-month (April 2015). A total of 668 SA clinical isolates were collected, resulting in an overall incidence rate of SA total-infections (TI, including invasive and non-invasive) of 49.1/100,000 monthly visits, with a range of 32.6–90.1 (Supplementary Table SS1). The median age of patients was 27 years (range: 1 month to 96 years), with 251 (37.5 %) being children (<19 years) and 274 (41 %) females (Table 2 and Supplementary Table SS2).

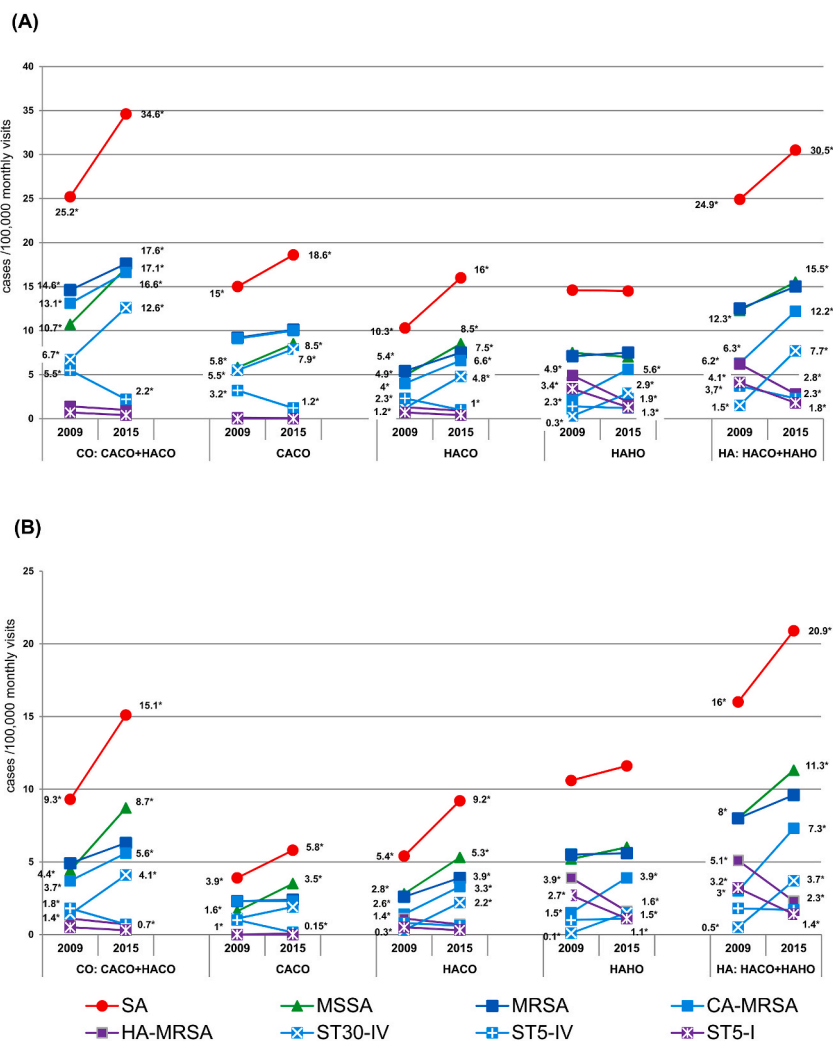


Fig. 2. Incidence of cases of (A) total and (B) invasive infections caused by *S. aureus* (SA), MSSA, MRSA and MRSA genotypes (including CA-MRSA_G and HA-MRSA_G and major MRSA clones) by onset type and epidemiological criteria (CDC) of infections, 2009 and 2015, Argentina. **Abbreviation:** n*: $P < 0.05$ by χ^2 test for the comparison between 2009 and 2015 of infections incidence, by onset type and epidemiological criteria (CDC) of infections.

Incidence: Number of cases/100,000 monthly visits. Number of visits (V): include outpatient facility, emergency service and admissions during one month.

Most cases were community-onset (CO) infections (471/668, 70.5 %), both in pediatrics (170/251, 67.7 %) and adults (301/417, 72.2 %, [Tables 3 and 4](#)). Of all SA infections, 341 cases (51.0 %, 95 % CI: 47.2 %–54.8 %) were caused by MRSA.

Most SA infections were HA (HACO and HAHO), totaling 415 cases (62.1 %) with an incidence rate of 30.5/100,000 ($P < 0.0001$, [Supplementary Table SS3](#)).

Among 668 patients, there were 817 SA infections: 41.4 % SSTI (34.5 % uncomplicated, 6.9 % complicated), 22.5 % bacteremia, 9.2 % lower respiratory tract infections, and 8.2 % musculoskeletal infections, [Supplementary Table SS2](#) provides additional details.

Among all patients, 55.1 % experienced invasive infections, with INVI cases more prevalent among MSSA infections (61.4 %, 201 out of 327) compared to MRSA infections (47.5 %, 162 out of 341), primarily attributed to musculoskeletal infections ([Supplementary Table SS2](#)).

b) Genotyping of MRSA strains and infections

The majority of MRSA isolates (88.6 %, 302/341) were classified as CA-MRSA_G, with 11.4 % as HA-MRSA_G ([Table 1](#)). Molecular characteristics, such as CC, ST, MLST, PFGE type and subtype, *spaA* and *SCCmec* types, presence of *pvl* genes, *agr* allotype, virulence gene profiles, and drug resistance patterns for both CA-MRSA_G and HA-MRSA_G, are detailed in [Table 1](#). Prevalence and overall incidence data for TI and INVI caused by SA, MSSA, MRSA, HA-MRSA_G, CA-MRSA_G, and major MRSA clones from this study are compared with data from the previous one [12], covering the entire population and stratified by age groups, onset type (community or hospital), and epidemiological classifications of infections [CACO or CA, HACO, HAHO, HA (HACO + HAHO)] are shown in [Tables 2–4](#), [Figs. 1–2](#), and [Supplementary Table S3](#) and [Figs. S1–S2](#).

Among CA-MRSA_G isolates (86 %, 259/302), two major clones predominated. The PFGE-type N-ST30-SCCmecIV accounted for 70.2 % (212/302), and the PFGE-type I-ST5-IV-SCCmecIV comprised 15.6 % (47/302) ([Table 1](#)). The remaining CA-MRSA_G isolates belonged to the following genotypes: PFGE-USA300-ST8-IV-LV (6 %, n: 18/302), PFGE-D-ST97-IV (4 %, n: 12/302), PFGE-R-ST72-IV (3.3 %, n: 10/302), PFGE-Y-ST509-IVa (0.7 %, n: 2/302), and PFGE-QQ-ST1649-IV (SLV of ST6, one isolate) ([Table 1](#)). For HA-MRSA_G isolates (n: 39), the Cordobes/Chilean clone, PFGE-A-ST5-SCCmecI, predominated (61.5 %, n: 24/39). The second most identified HA-MRSA_G was the Pediatric clone Argentinean variant (PFGE-C-ST100-SCCmecINv) (38.5 %, n: 15/39) ([Table 1](#)).

Furthermore, CA-MRSA_G showed significantly higher rates of TI [22.2 vs. 2.9, $P < 0.0001$, OR (95 % CI): 13.3 (9.32–18.99)] and INVI [9.6 vs. 2.4, $P < 0.0001$, OR (95 % CI): 4.06 (2.77–5.97)] infections per 100,000 monthly visits compared to HA-MRSA_G, primarily due to the increased rate of CA-MRSA ST30-IV clone (15.6), surpassing rates of other major MRSA clones ([Table 2](#)).

c) SA infections cases: MSSA, MRSA and MRSA Genotypes

In reference to SA, MRSA and MSSA infection incidence rates stratified by age groups ([Table 2](#)), we found similar overall TI rates for MSSA and MRSA in the entire population (24.0 vs. 25.1, $P = 0.5889$) and in adults (25.4 vs. 21.9, $P = 0.1289$). However, MRSA showed a higher TI rate in children (30.8 vs. 21.4, $P = 0.0045$, OR: 1.44), especially in non-INVI cases where INVI rates were comparable ($P = 0.6494$). This difference was evident in CO and CACO infections ([Table 4](#)). Conversely, there was a higher incidence of INVI caused by MSSA than by MRSA in the entire population (14.8 vs. 11.9, OR:1.24), especially in adults (15.7 vs. 11.8, OR:1.33), particularly in those older than 30 years ([Table 2](#) and [Supplementary Table S2](#)), and among CO infections [entire population (8.7 vs. 6.3, OR:1.38, [Table 3](#)) and adults (9.8 vs. 6.2, OR:1.60, [Table 4](#))].

Comparing infection rates across age groups, we observed similar TI and INVI rates caused by SA and MSSA in pediatrics and adults. However, a higher incidence of MRSA-TI was identified in pediatrics (particularly in patients aged 1–18 years) than in adults (30.8 vs. 21.9, OR: 1.44), especially non-INVI cases, in the community setting and linked to CA-MRSA ST30-IV clone ([Table 2](#), [Supplementary Fig. S1](#) and [Table S2](#)).

d) SA infections: CO vs. HO infections:

For CO- and HO- SA infections, the community displayed higher overall incidences of SA, MRSA, and MSSA than the hospital ([Table 3](#)). The elevated TI and INVI incidences caused by SA and MSSA were observed in adults, especially in HACO invasive infections (SA-HACO: 10.7 vs. SA-CACO: 5.3, MSSA-HACO: 6.4 vs. MSSA-CACO: 3.4, [Table 4](#)).

Conversely, a higher MRSA-TI incidence in the community than in the hospital (17.3 vs. 7.5) [with comparable MRSA proportions between CO-TI (50.8 %) and HO-TI (51.8 %) ($P = 0.86$), [Table 3](#)] was linked to non-invasive MRSA infections, as MRSA-INVI rates were similar ($P = 0.43$, [Table 3](#)). This finding was observed in both pediatric and adult patients ([Table 4](#)), primarily related to a higher CA-MRSA-ST30-IVc (non-INVI)-TI rate in the community (CO: 12.6 vs. HO: 2.9, $P < 0.0001$), especially in CACO (non-INVI)-TI ([Table 3](#)).

In reference to INVI, while overall MRSA and CA-MRSA_G INVI rates were comparable between community and hospital settings, significant clonal-level differences were identified ([Table 3](#)). In the community, ST30-IV clone caused a higher INVI rate than CA-MRSA-ST5-IV (4.1 vs. 0.73, OR 5.6), with comparable rates in CACO (1.9) and HACO (2.2) infections, $P = 0.59$ across both age groups. Conversely, in the hospital, INVI rates caused by HA-MRSA ST5-I (1.1) and CA-MRSA clones (ST30-IV/1.5, ST5-IV/1.1) were comparable, especially in adults ([Tables 3 and 4](#)).

e) SA infections: HA vs. CA infections

Regarding HA (HAHO and HACO) and CACO SA infections (Supplementary Table S3), higher SA (MSSA and MRSA) infection rates (TI and INVI) were found in HA compared to CA infections (SA, TI: 1.64 fold, INVI: 3.6 fold; MSSA, TI: 1.80 fold, INVI: 3.3 fold; MRSA, TI: 1.50-fold, INVI: 4.1-fold) with comparable rates between HACO and HAHO infections (Table 3).

The higher MRSA TI and INVI rates in HA infections compared to CACO (Supplementary Table S3) were attributed to *i*) a higher CA-MRSA_G INVI incidence, mainly associated with both CA-MRSA clones (with similar INVI rates between HACO and HAHO infections): ST30-IV and ST5-IV clones, alongside other CA-MRSA clones (USA300-LV and ST97-IV) (Table 3), and *ii*) a greater HA-MRSA_G TI and INVI incidence, linked to ST5-I and ST100-IVNv clones and HAHO infections, particularly in adults (Table 3 and Supplementary Table S3). Notably, in HA MRSA infections (HACO and HAHO), CA-MRSA_G showed higher rates than HA-MRSA_G (Supplementary Table S3).

3.2. Evolution of SA infections (longitudinal retrospective study): 2009 vs. 2015

1) All Epidemiologic classes and age group

In Argentina, total and invasive SA infection rates increased by 23.4 % (from 39.8 to 49.1, OR: 1.2) and 31.2 % (from 19.9 to 26.1, OR: 1.3), respectively, from 2009 to 2015 in the entire population. These increases were driven by a 32.5 % rise in MSSA TI (from 18.1 to 24.0, OR: 1.3) and a 54.2 % growth in MSSA INVI (from 9.6 to 14.8, OR: 1.5), mostly in adults, while MRSA infection rates remained stable [Fig. 1 (A, B), Table 2, Supplementary Table S4]. This stability in adults was linked to a CA-MRSA-ST30-IV rates increase and a HA-MRSA-ST5-I rates decrease. Notably, CA-MRSA-ST5-IV rates unchanged [Table 2, Fig. 1 (A, B), Supplementary Table S4].

In pediatrics, there was a 26.7 % increase in MRSA-TI incidence (24.3–30.8, OR:1.4), particularly non-INVI, while MSSA infection rates remained unchanged [Fig. 1 (A, B), Table 2, Supplementary Table S4]. This rise was linked to a CA-MRSA-ST30-IV clone rates increase and a CA-MRSA ST5-IV rates decline, [Table 2, Fig. 1 (A, B), Supplementary Table S4].

2) Community-onset cases, (CACO and HACO)

Community-onset SA TI and INVI rates rose by 37.3 % (25.2–34.6, OR: 1.4) and 62.4 % (9.3–15.1, OR: 1.6) in this period. This increase was related to *i*) a rise in CO-MSSA TI and INVI incidence [59.8 % (10.7–17.1, OR: 1.6) and 97.7 %, (4.4–8.7, OR: 1.9) respectively, Table 3, Fig. 2 (A, B)], detected in both HACO and CACO MSSA infections, especially in adults (for children, only a significant increase in CACO MSSA INVI incidence was noted, Table 4), and *ii*) a rise in CO MRSA TI overall rate [20.5 %, 14.6 to 17.6, OR: 1.2, Table 3, Fig. 2 (A, B)], particularly INVI in adults (82.3 %, 3.4 to 6.2, OR: 1.8, Table 4), and among HACO infections. The increase in CO-MRSA infection incidence was primarily driven by the CA-MRSA-ST30-IV clone, while CA-MRSA-ST5-IV community-onset TI and INVI rates remained unchanged (mainly in adults in HACO and CACO infections) or decreased (mainly in children among CACO TI and INVI and HACO non-INVI TI), [Tables 3 and 4, Fig. 2 (A, B) Supplementary Table S4].

3) Hospital-onset cases, (HAHO)

Between 2009 and 2015, overall rates of HAHO SA TI and INVI remained stable in the entire population and among adults for both MRSA and MSSA infections (Tables 3 and 4, Fig. 2). Notably, there was a 70.4 % increase in pediatric HAHO MRSA TI, (5.4–9.2, OR: 1.7), especially in non-invasive MRSA infections like uncomplicated skin and soft tissue infections (Table 4, Supplementary Table S4).

The HAHO CA-MRSA_G TI and INVI rates significantly increased in the entire population, with pediatrics predominantly experiencing non-invasive infections. This rise was mainly attributed to the hospital introduction and spread of the CA-MRSA-ST30-IV clone. The persistence of the CA-MRSA-ST5-IV clone and, to a lesser extent, other CA-MRSA clones such as USA300-LV and ST97-IV, also contributed to this evolution [Fig. 2 (A, B) Tables 3 and 4, Supplementary Table S4, and Fig. S2]. Furthermore, a displacement of the traditional HA-MRSA_G, particularly the HA-MRSA-ST5-I clone, by the CA-MRSA clones was evidenced, primarily in adults, resulting in the stability of HAHO MRSA infections in this age group [Tables 3 and 4, Fig. 2 (A, B), Supplementary Table S4, and Fig. S2].

4) Healthcare associated Cases (HA: HAHO + HACO)

The overall rates of healthcare-associated SA TI increased by 22.5 % (24.9–30.5, OR: 1.2), and INVI increased by 30.6 % (16.0–20.9, OR: 1.3) during this period [Fig. 2 (A, B), Supplementary Table S3]. These increases were primarily driven by MSSA, showing a 26.0 % rise in TI (12.3–15.5, OR: 1.3) and a 41.3 % increase in INVI (8.0–11.3, OR: 1.4), mainly among adults with HACO infections. In the entire population and adults, healthcare-associated MRSA TI and INVI incidence remained unchanged. However, pediatric patients saw a significant 57 % increase (11.3–17.7, OR: 1.6, Supplementary Table S3) in MRSA TI (non-INVI) related to HAHO infections (Table 4 and Supplementary Table S4).

This evolution appears linked to decreased adult HAHO HA-MRSA_G infections, especially HA-MRSA-ST5-I. Concurrently, there's a notable rise in both HACO and HAHO TI and INVI infections by CA-MRSA_G strains in both age groups. This is driven by the increasing ST30-IV clone incidence in both TI and INVI cases, along with rising INVI rates of other minor clones (USA300-LV and ST97-IV), alongside sustained ST5-IV clone rates in INVI cases (Supplementary Tables S3 and S4).

3.3. SA infections by Argentina regions

In 2015, the prospective study revealed similar SA TI rates between the northern and southern regions (81.1 vs. 81.4, $P = 0.98$), both surpassing the central region (41.0, $P < 0.0001$). The disparity was due to higher MRSA (59.1) than MSSA (21.9) incidence in the North and higher MSSA (60.5) than MRSA (20.8) rates in the South ($P < 0.0001$, Table 5). MRSA infection rates were 3.0-fold higher in the North (59.1) than the Center (19.9) and 2.8-fold higher than the South (20.8) of Argentina ($P < 0.0001$), driven by major CA-MRSA clones, ST30-IV and ST5-IV, with the former showing a 4-5-fold higher rate than the latter clone in both regions. Other CA-MRSA clones (USA300-LV and ST97-IV) also contributed to this difference. In contrast, comparable HA-MRSA_G infection rates were found between the North (5.6) and South (5.2) of the country, particularly related to the ST5-I clone (3.9 vs. 5.2, Table 5).

From 2009 to 2015, in longitudinal analysis, the northern region exhibited stable TI incidence for SA, MSSA, and MRSA (including genotypes and major clones) (Supplementary Fig. S3). In the central region, overall SA infections increased by 18.2 % (34.7–41.0) and MSSA by 30.9 % (16.2–21.2), while MRSA rates remained steady (Table 5 and Supplementary Fig. S3). CA-MRSA_G infections rose by 41.6 %, linked to increased ST30-IV clone rates and decreased ST5-IV clone rates, primarily in the community (Supplementary Fig. S4). HA-MRSA_G infections declined by 63.3 %, driven by decreased ST5-I clone rates, replaced by the ST30-IV clone and other CA-MRSA clones (ST97-IV and USA300-LV) (Table 5 and Supplementary Fig. S4). In the southern region, SA infections increased by 40.3 % (58.0–81.4), mainly due to a 47.2 % rise in MSSA (41.1–60.5), with stable MRSA (genotypes and major clones) rates, except for increased ST30-IV clone rates (Table 5 and Supplementary Fig. S3).

3.4. Antimicrobial resistance to non-β-Lactam agents

In 2015, CA-MRSA_G had lower resistance than HA-MRSA_G, consistent with 2009 [12] ($P < 0.0001$, Supplementary Table S5). Multi-resistance was exclusive to HA-MRSA_G as seen in our previous studies [12,13,25–27]. All MRSA isolates were susceptible to teicoplanin, linezolid, and vancomycin (MIC90: 1 μg/mL, range: 0.5–2 μg/mL). Except for one CA-MRSA ST30-IV isolate with high-level mupirocin resistance (MuH, MIC: >1024 μg/mL, *mupA*⁺), MRSA isolates were mupirocin-sensitive (MIC90: 0.38 μg/mL, range: 0.094–0.5 μg/mL) (Table 1), and mupirocin resistance was only 0.3 % (95%CI: 6.2–9) (1/341 MRSA). The ST30-IV clone showed lower CLI and ERY resistance than ST5-IV, decreasing from 2009 to 2015 (Supplementary Table S5). With increased community-onset MSSA infections (2009–2015), resistance rose significantly to GEN (4.4 %–12.5 %), ERY (8.2 %–15.9 %), and CLI (3.8 %–11.6 %, especially CLI: 1.3 %–8.2 %) (Supplementary Table S5). Among 66 ERY-resistant MSSA isolates, CC8 (28.8 %), CC398 (15.1 %), CC30 (15.1 %), CC45 (10.6 %), and CC5 (9.1 %) were most frequent lineages. CC398-t1451-*ermT*⁺ was exclusive to 2015, constituting 21.7 % of ERY-resistant MSSA. All CC398-MSSA isolates (n: 10) were *pvl*-negative and harbored *scn* gene, indicative of IEC system, with IEC types C (n: 6) and B (n: 4) (Supplementary Table S6).

4. Discussion

Notably, few studies provide information on MSSA and MRSA infection epidemiology, prevalence, and incidence evolution [15, 18–20], including shifts in major MRSA clones and their correlation with antimicrobial resistance, both in the general population and across age groups [34–37]. This study is the first nationwide report on the evolving incidence of MSSA and MRSA infections in Argentina, highlighting on major MRSA clones causing community and hospital-onset infections across age groups. In the national prospective study in 2015, MRSA constituted 51.0 % of SA isolates, with an overall TI rate of 24.0/100,000 monthly visits, remaining stable since 2009. In contrast, CO MSSA INVI incidence rose, with increased erythromycin resistance linked to the emergence of MSSA CC398-t1451-*ermT*⁺

Concerning MRSA genotypes, our results align with previous studies [12,13], showing higher infections rates (over 10-fold) for typical CA-MRSA_G compared to classic HA-MRSA_G, especially in non-invasive infections. The molecular characteristics and non-β-lactam drug resistance shared by isolates from each HRC (CA-MRSA clones: ST30-IV, ST5-IV, USA300-LV, and ST97-IV; HA-MRSA clones: ST5-I and ST100-IVNv) correspond to prior reports [12,13]. Recent genomic epidemiology data from Latin America in 2019³⁸ align with our results. Moreover, the association of different clonal backgrounds with distinct antibiotic resistance and virulence gene profiles is consistent with other studies [12,13,38,39]. Genetic characteristics of CA-MRSA ST30-IV-t019 isolates suggest affiliation with the ARG4 phylogenetic clade, identified in a recent study of CC30 MRSA strains in Argentina [40]. Considerably, this clone had the highest incidence, surpassing the other major clones CA-MRSA/ST5-IV and HA-MRSA/ST5-I. However, incidence rates varied across infection epidemiological classes, patient age groups, and regions, which is crucial insights for guiding MRSA control strategies.

The overall incidence rates of MSSA and MRSA TI were comparable across the entire population and adults. However, MRSA TI rates, particularly non-INVI, were 1.4 times higher in children (1–18 years) compared to MSSA TI rates. This discrepancy was more pronounced in the community setting (1.6 times higher) and CACO infections (1.7 times higher). These results, consistent with previous studies [12,14,15,41], underscore the heightened risk of CA-MRSA non-invasive infections, especially SSTIs, in children, associated with the CA-MRSA-ST30-IV clone. Conversely, in adults over 30, MSSA invasive infections surpassed MRSA (1.3-fold), notably in musculoskeletal cases and the community (1.6-fold). In line with previous studies from the US and European countries [14, 15,18–20,35,37], these findings highlight higher MSSA invasive infection rates than MRSA and variations based on infection site and population characteristics such as patient age.

Additionally, although MRSA proportions were comparable between the community (50.7 %) and the hospital setting (51.8 %), higher SA TI and INVI incidence rates were detected in the community. This was linked to increased CO-MSSA TI and INVI, especially HACO-MSSA TI and INVI in adults, and higher CO-MRSA infection rates, particularly non-INVI, in both age groups. These findings

underscore the importance of targeting not only hospitals but also the community in strategies to control SA transmission [15,18]. The CA-MRSA-ST30-IV clone drove higher incidence of MRSA TI, especially non-INVI, in the community versus the hospital, notably in CACO infections in both age groups. However, MRSA INVI rates were similar between community and hospital settings. In the community, the CA-MRSA-ST30-IV clone caused the highest INVI incidence, with comparable rates between HACO and CACO infections in adults and pediatrics. In the hospital, this clone exhibited similar INVI rates to other major CC5 MRSA clones (CA-MRSA-ST5-IV and HA-MRSA-ST5-I). These findings underscore different behaviors of two key CA-MRSA clones in community and hospital settings, indicating that unique capacities or characteristics may contribute to their success in these settings, consistent with previous reports [11,13,42–44]. Beyond genetic traits [11,45,40], these clones might have distinct environmental reservoirs and colonization patterns [11,13], impacting their transmission capacity differentially. However, additional studies are needed to confirm this hypothesis.

In Argentina, HA SA infections, particularly invasive cases, caused by both MSSA and MRSA, were over 3 times higher than CA infections. MRSA's higher incidence in HA infections was mainly driven by CA-MRSA clones (with similar INVI rates between HACO and HAHO infections), particularly the ST30-IV and ST5-IV, alongside other CA-MRSA clones (USA300-LV and ST97-IV). Traditional HA-MRSA_G, like ST5-I and ST100-IVNv clones in adults, contributed but to a lesser extent than CA-MRSA clones. These results confirm the infiltration and transmission of CA-MRSA clones in Argentine hospitals, consistent with the previous study [13]. The dissemination of these MRSA clones, along with MSSA, is likely influenced by their virulence and fitness, as well as varying healthcare interventions, differing between high-income countries and low- and middle-income countries like Argentina, with limited resources and a higher burden of HA infections [4,23,46,47].

Importantly, as reported previously [12,13], multidrug resistance patterns were exclusive to HA-MRSA_G. The CA-MRSA ST30-IV clone consistently showed lower resistance rates to erythromycin and clindamycin compared to ST5-IV counterparts throughout the analyzed period. However, a longitudinal analysis via the WHONET Argentina Network in 2018–2022 [24] revealed a slight increasing trend in resistance to ERY and CLI among MRSA isolates, highlighting the need for continuous surveillance for MRSA treatment alternatives in community and hospital settings. Additionally, one CA-MRSA ST30-IV clone isolate with mupirocin resistance (MuH, encoding by *mupA*) was identified, constituting 0.3 % (95 % CI 0.054–1.654) of clinical MRSA isolates nationwide. Notably, the mupirocin resistance prevalence in Argentina (0.3 %) falls within the lower range compared to European (0.3%–98.0 %), North American (0.5%–30.0 % or more), and Asian (0%–75.0 %) countries [48–52]. A genomic study of CC30 MRSA strains from Argentine provinces also detected mupirocin resistance associated with the ST30-IV clone [40]. These findings support the potential for transmission of these resistance determinants (*mupA* or *mupB* genes) through plasmids, which can also carry resistance genes to other antimicrobials across major SA lineages (CC5, CC8, CC22, and CC30) in both human and animal populations [48,49,51,52]. Therefore, ongoing surveillance and a strict mupirocin use policy are recommended in Argentina.

On the other hand, the highly successful CC5 lineage, other prominent MRSA lineage in Argentina [12,13,26], has shown potential for complex competitive interactions, including the acquisition of multidrug resistance, vancomycin resistance, and diverse SCC_{mec} types [9,53]. This lineage has undergone dynamic regional evolution, leading to specific sublineages with genomic changes associated with increased antibiotic resistance and decreased virulence [39,54–56]. Notable examples in this region include the spread of the CC5/ST105-II-t002 multidrug-resistant MRSA clone in Rio de Janeiro, Brazil [57], a neighboring country to Argentina. In Argentina, two HA-MRSA clones (CC5/ST5-I-t149, CC5/ST100-IVNv-t002) and one CA-MRSA clone (CC5/ST5-IV-t311 and related) have been circulating since the 2000s [12,26,58]. Previous reports in this country have also indicated that the CA-MRSA ST5-IV clone expresses h-VISA or VISA phenotypes [27,59,60], or exhibits reduced-susceptibility to tigecycline [61]. These findings underscore the need for global molecular surveillance of CC5 MRSA HRCs.

Regarding the evolution in the incidence of SA infections in Argentina, SA total and invasive infection rates increased by 23.4 % and 31.2 %, respectively, from 2009 to 2015. This rise was driven by a 32.5 % increase in MSSA TI and a 54.2 % increase in MSSA INVI, mainly in adults. The majority of the MSSA increase was in community-onset MSSA TI (59.8 %) and INVI (97.7 %), including both HACO-MSSA and CACO-MSSA infections, especially in adults, although in children an increase in CACO MSSA INVI incidence was also noted. Our findings suggest that the overall burden of community-onset MSSA infections is rising in Argentina, contributing to the SA disease burden, with no significant MRSA changes. This pattern aligns with recent data from North America and Europe, including bloodstream and SSTI infections [15,18–20,22,35]. Importantly, our study has revealed a simultaneous increase in CO-MSSA infections and resistance to non-β-lactam antibiotics, specifically erythromycin, linked to the emergence and spread of the MSSA-CC398-t1451-*ermT*⁺-IEC⁺-*pvl* lineage in Argentina. Another WHONET Argentina Network analysis [24] has identified a significant rise in the MSSA relative proportion of total SA infections from 50.5 % (5720 culture-confirmed SA infections) in 2009 to 66.9 % (6278 culture-confirmed SA infections) in 2021, along with increased resistance to non-β-lactam antibiotics (clindamycin, erythromycin, and gentamicin). These findings support our longitudinal study data, suggesting a continuous increase in MSSA infections accompanied by the resistance to ERY, CLI and GEN since 2009, including the impact of the COVID-19 pandemic. Furthermore, in a recent study [45], the MSSA-CC398-t1451-*ermT*⁺ was detected as the predominant MSSA lineage in bloodstream isolates across Latin America's southern cone countries, including Argentina, during 2019. CC398 is a highly transmissible lineage, associated with both livestock (LA-MRSA) and humans (HA-MSSA). These two phylogenetic clades, LA and HA, exhibit genomic differences, particularly in mobile genetic elements acquisition or loss, influencing host adaptation, antimicrobial resistance and virulence. The HA-ST398-MSSA lineage, globally disseminated, is characterized by macrolide resistance, *spa* types *t571* or *t1451*, and the IEC cluster presence, linking it to a human origin, in the majority of isolates [62,63]. Our study suggests that, in Argentina, this highly transmissible MSSA-CC398-t1451-*ermT*⁺-IEC⁺-*pvl* lineage likely initiated its spread during 2009–2015, driving the increase in macrolide resistance among MSSA infections.

Notably, due to limited evidence on MSSA horizontal transmission, most studies have focused on the importance of transmission

control measures with vertical or MRSA-targeted approaches, such as active surveillance or MRSA decolonization [64]. Nevertheless, considering MSSA potential growing role as a healthcare-associated invasive pathogen, especially in community-onset infections, as indicated by our study in Argentina and other research globally [15,18,19,22,63,65,66], reassessing and thoroughly studying MSSA epidemiology (general and molecular) is advisable for formulating effective control strategies.

On the other hand, the sustained rates of MRSA TI and INVI during this period, particularly in adults, are associated with the stability of HAHO MRSA infections, reflecting an evolution already identified in other countries [18,22]. In Argentina, this stability is linked to the replacement of HA-MRSA-ST5-I (previously linked to HAHO MRSA infections in adults [25,58]) by CA-MRSA ST30-IV and other clones like USA300-LV and ST97-IV. In adults, CA-MRSA-ST30-IV supplements rather than replaces CA-MRSA ST5-IV, particularly in HA (HAHO and HACO) infections. Consequently, while HAHO MRSA infections remained stable in adults, CO MRSA total infections increased (20.5%), driven by a rise in INVI cases (82.3%), primarily due to increased HACO MRSA INVI. Contrastingly, MRSA TI rates in children increased by 26.7%, primarily due to a 1.7-fold rise in HAHO-MRSA TI, driven by CA-MRSAG (non-INVI)-TI associated with the spread of the CA-MRSA ST30-IV clone in hospitals. This, along with the ST5-IV clone, contributed to the surge in HAHO MRSA infections in children, confirming our previous study [13] emphasizing the high risk of CA-MRSA_G colonization and acquisition in children aged 1–18 years in hospitals.

The need for reinforced strategies to control HAHO MRSA infections, particularly in children, is underscored once again [12,41,65,67]. On the other hand, the CO MRSA infections rates in children remained consistently higher than MSSA infections and stable from 2009 to 2015. This stability was linked to the ST30-IV clone spread, displacing the CA-MRSA ST5-IV clone in CACO infections (TI and INVI) and HACO non-invasive infections. These findings suggest that the distinct behavior of MRSA clones is influenced by both the infection setting (hospital or community), reflecting differences in transmission capacity, and associations between SA genotypes and patient age, as observed in certain SA lineages [12,57,68].

All these results demonstrate that the increase in SA infections during this period was primarily driven by a rising evolution over time in community-onset SA infections, particularly in adults, related to increased rates of HACO-MSSA and HACO-MRSA infections and a rise in CACO-MSSA infections in both age groups. Conversely, the stability in HAHO SA infections, mainly in adults, and the decreasing MRSA proportion during 2018–2021, as shown by the WHONET database [24], could be attributed to diverse hospital infection control strategies implemented in Argentina (<http://www.vihda.gov.ar/>). This suggests more effective infection control practices in hospitals compared to the community, aligning with trends reported in some European Union countries [14,15] and the US [18]. Alongside current hospital strategies like contact precautions, it's crucial to consider non-specific approaches for MRSA and focus infection control on SA (MRSA and MSSA) to disrupt the transmission chain between hospitals and communities [18,65,69], considering it as a One Health issue encompassing humans, the environment, animals, and plants [1,10,70].

The countrywide coverage of this study allowed for detecting similar rates of SA infections in the northern and southern regions, both higher than in the central region of Argentina. The North had a higher MRSA incidence (59.1) than MSSA (21.9), while the South exhibited a higher MSSA incidence (60.5) than MRSA. The MRSA infections rates were comparable between the central and southern regions, but the northern region had a consistently higher MRSA incidence (2–3 fold), mainly due to elevated CA-MRSA_G rates, particularly ST30-IV, although ST5-IV, USA300-LV, and ST97-IV also contributed. These findings suggest that in the North, specific weather conditions (warmer and/or more humid) and socio-demographic factors (overcrowding, low income, among others) would contribute to the spread of CA-MRSA clones, aligning with other studies [71–73]. Conversely, the sparsely populated South, with different weather conditions (cooler and/or drier), has higher MSSA incidence than other regions of Argentina. Furthermore, while MSSA and MRSA infections rates remained stable in the North between 2009 and 2015, the Centre and the South experienced SA infection rate increases (18.2% and 40.3%, respectively), driven by rising MSSA rates (30.8% and 47.2%, respectively). In line with other studies [15,20,66], these results support the hypothesis that MRSA and MSSA don't compete for the same ecological niche. Then, different factors, including weather conditions, socio-demographics, antibiotic use rates, and the unique genetic background of each clone, may favor the transmission of MSSA or MRSA. Consequently, MRSA and MSSA do not inevitably replace each other.

Significantly, most changes in MRSA clone infections rates occurred in the central region, where the hospital entry of the ST97-IV clone, causing HAHO infections, was identified. This clone, also identified as a minor colonizer during hospital admissions in Córdoba in a prior study [13], is likely genetic related to livestock-associated MRSA (LA-MRSA), CC97 [9,74]. The central region, Argentina's primary agricultural and livestock area [75], would require further studies to investigate livestock as a possible reservoir of this lineage in Argentina.

In conclusion, our study has identified an increasing burden of SA infections in Argentina from 2009 to 2015, predominantly in the central and southern regions, driven by a rise in community-onset infections. This surge was primarily attributed to growing rates of MSSA infections, accompanied by increased resistance to macrolides and gentamicin, while the proportion of MRSA remained stable. The emergence and spread of the erythromycin-resistant MSSA CC398-t1451 lineage contributed to this evolution, adding to the overall burden of invasive SA disease. The rise in SA infections was associated with increased rates of HACO MRSA and HACO MSSA total and invasive infections in adults, as well as a rise in CACO MSSA infections across age groups. Conversely, CACO MRSA infections remained stable. While overall rates of HAHO MRSA infections showed no significant changes in the entire population and adults, there was a notable 1.7-fold increase in children, contributing to the overall rise in healthcare-associated (HA) SA infections. Our study also identified the entry and spread of the ST30-IV clone in hospitals, along with other CA-MRSA clones (USA300 LV and ST97-IV). Importantly, these clones complemented rather than replaced the ST5-IV clone in HA (HACO and HAHO) invasive infections in both age groups, with the ST30-IV clone displacing the HA-MRSA ST5-I clone, particularly in adult HAHO infections.

The strengths of this study include: *i*) the first-time assessment of overall SA disease incidence throughout the country. *ii*) a prospective 2015 study with a retrospective longitudinal investigation comparing SA infection incidence between 2015 and the previous 2009 study [12], *iii*) molecular characterization of isolates with sociodemographic and clinical patient data. Both studies (2009 and

2015) covered hospitals distributed nationwide (most from WHONET Argentina Network), serving 3.5 % of the Argentine population [76]. Importantly, the analysis has also been stratified by age groups, epidemiological classes, and country regions.

The main limitation of the comparative study is the relatively short inclusion period for infection cases in each study (one month). Monthly values of the pooled estimated incidence rates were compared across all surveillance sites. The limited number of monthly cases may have led to underpowered statistical analysis, potentially missing changes in incidence rates, especially for minor clones. However, the identified changes were sufficient to demonstrate increases or decreases in the burden of MRSA, MSSA, and principal MRSA clones. Furthermore, the analysis involved only two points separated by 6 years, lacking consecutive intermediate points to demonstrate a continuous trend throughout the period. Nevertheless, the annual results of the national surveillance on antimicrobial resistance evolution [24] provided by the WHONET Argentina Network (to which most of the hospitals that participated in both studies belong) align with the evolutionary results on MRSA and MSSA infections from our longitudinal analysis, supporting the continuity of this evolution until at least the year 2021. Additionally, for comparability between the results of both studies, 85 % of the hospitals participated in both studies, with only an 8.3 % difference in the populations served.

The analysis of MRSA and MSSA incidence in Argentina adds to existing literature, underscoring the community's role as a growing reservoir for successful MSSA and CA-MRSA clones, resulting in healthcare-associated community-onset infections. These findings provide valuable insights for improving *S. aureus* infection prevention and control programs, guiding transmission control priorities in Argentina and globally, and addressing antimicrobial resistance on a global scale.

Funding statement

This work was supported by the National Council for Scientific Research and Technology of Argentina (CONICET-PIP-2014-2018 to CS), Agencia Nacional de Promoción Científica y Tecnológica, Argentina (ANPCyT-PICT 2017-0554 to CS and PICT 2020-02171 to CS) and Secretaría de Ciencia y Técnica-Universidad Nacional de Córdoba (SECyT-UNC) to CS. EB and MJG are fellow recipient of the ANPCyT, DB is a fellow recipient of CONICET. CS and JB are career investigator members of CONICET.

Data availability statement

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Danilo Barcudi: Writing - original draft, Investigation, Formal analysis, Conceptualization. **Enrique Blasko:** Writing - review & editing, Methodology, Investigation, Formal analysis. **María José Gonzalez:** Methodology, Investigation. **Paula Gagetti:** Investigation, Conceptualization. **Ricardo Lamberghini:** Investigation, Conceptualization. **Analia Garnerio:** Investigation, Conceptualization. **Claudia Sarkis:** Investigation. **Diego Faccone:** Investigation. **Celeste Lucero:** Investigation. **Dario Tosoroni:** Investigation. **Study Group of *S. aureus* in Argentina:** Investigation. **Jose Luis Bocco:** Writing - review & editing, Writing - original draft, Investigation, Conceptualization. **Alejandra Corso:** Writing - review & editing, Writing - original draft, Investigation, Formal analysis, Conceptualization. **Claudia Sola:** Writing - review & editing, Writing - original draft, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to thank all investigators of the Study Group of *S. aureus* in Córdoba Argentina who have participated in this study.

The participating investigators and institutions are as follows:

Noemí Borda de Notario, Joaquín Bermejo, (ABC Hospital Español de Rosario, Rosario, Santa Fe); Silvia Mariela Farfan, Patricia Carrizo Herrera (Hospital de Niños de Catamarca); Elida Pallone, Gabriela Neumann, Marisa N. Almuzara (Hospital Interzonal de Agudos Eva Perón, San Martín Buenos Aires), Edith Dinerstein, Marcelo Gañete, Ana María Togneri (Hospital Interzonal General de Agudos "EVITA", Lanús, Buenos Aires); Patricia Andres, Elizabeth Madsen (Hospital Universitario Fundación Favaloro, CABA); Damian Aguila, Jorgelina F. Perez., Patricia Marchiaro (Hospital Provincial el Centenario, Rosario, Santa Fe); Nora Orellana, Marcelo del Castillo (Hospital Fleni, CABA); María Rosa Baroni, Gustavo Cesar Ezcurra, (Hospital de Niños Dr Orlando Alassia, Santa Fe); Flavia Amalfi y Olivia Gear (Hospital Parmenio Piñero, CABA); Nancy N. Pereira, María T. Occello (Hospital Central de Formosa, Formosa); Guillermo R García, Josefina M Villegas, Jorge Gonzalez Nizzo (Hospital Zonal Padre Tardivo, Caleta Oliva, Santa Cruz); Marcelo Toffoli, Gabriela Granados, María R. Miranda (Hospital de Niños "Dr. Hector Quintana", Jujuy); Ana M. Pato, Fernando Achinelli (Hospital Angela Iglesias de Llano, Corrientes); Gladys Margarita Almada, Ana Laura Sanchez, Nuria Martina Gouts (Hospital Dr. Lucio Molas, Santa Rosa, La Pampa); Marcela Vargas, Edgar Adan Vega (Hospital Regional Río Grande "Nuestra Señora de la Candelaria", Río Grande, Tierra del Fuego); Cinthia Vázquez, Hortensia Cano (Hospital Regional Río Gallegos, Santa Cruz); Norma Esther Cech, Sergio Rodriguez, (Hospital "4 de Junio- Ramon Carrillo", Roque Saenz Peña, Chaco); Patricia Montanaro, Marisa Paredes, Analía V.

Garnero (Hospital de Niños de la Santísima Trinidad, Córdoba); Viviana Vilches, Rodolfo Quiros, Alejandro Cané, Macarena Uranga (Hospital Universitario Austral, Pilar, Buenos Aires); Liliana González, María Lucrecia Sanchez, Eugenia Tirao, (Hospital Infantil Municipal de Córdoba, Córdoba); Mónica Machain, Hugo Fleitas (HIGA Dr. Abraham Piñeyro, Junín, Buenos Aires); Norma Cudmani Blanca Mena (Sanatorio Rivadavia, Tucumán); Marisa Alejandra Lacono, María R. Núñez, María Martha Schinchirimini (Hospital Castro Rendón, Neuquén); Héctor Abate, Beatriz García (Hospital Pediátrico Dr. Humberto Notti, Guaymallén, Mendoza); María Luz Benvenutti, Laura Giordano (HIGA "Dr Jose Penna", Bahía Blanca, Buenos Aires); Juan Carlos Daniel Morales, Cecilia Vescina, (Hospital Sor María Ludovica, La Plata, Buenos Aires); Adriana Di Bella, Gabriela Taponier, Lucia Daciuk, Gabriela Degregoris (Hospital Nacional Profesor Alejandro Posadas, El Palomar, Buenos Aires); Leonardo Marianelli, Teresa Lopez, Marcelo Martins, Lidia Wolff (Hospital Rawson, Córdoba); Silvia G. Amador, Carina Evangelina Segovia (Hospital San Vicente de Paul, Salta); Lilia Camisassa, Luciana Sosa (Hospital Domingo Funes, Santa María de Punilla Córdoba); Sonia Flores, Eduardo Rombola (Hospital Dr. Enrique Vera Barros, La Rioja); Ana M. Gasparotto, Valeria Ocaña Carrizo, Carlos Quinteros Greco, Estefanía Ballari (Hospital Nacional de Clínicas, Córdoba); María J Minoli, Alicia Garutti, Valentina Cumiberti (Hospital Córdoba, Córdoba); Elda Díaz, Marcos Ciarlantini, José Gonzalez, (Hospital Militar Regional Córdoba); Ivana Lis Herrero, Ivana Ocampo, Adriana Lopez (Hospital Municipal de Urgencias, Córdoba); Paulo R Cortes, Patricia González, Miriam Calvari (Hospital Pediátrico del Niño Jesús, Córdoba); Andrea Piersigilli, Liliana Ether María Bilbao, Marcos Ciarlantini, Facundo Blanco (Sanatorio Aconcagua, Córdoba); Laura Decca, Claudio Manchado Fernando Riera, Graciela Beccerica, Daniela Vega (Clínica Regional del Sud, Córdoba); Liliana Fernández Canigia, Cristina Freuler, María Paula Della Latta, Micaela Mayer-Wolf (Hospital Aleman, CABA); Diego Yahni, Jorgelina Smayevsky, Laura Scocozza (CEMIC, CABA); María Susana Diaz, Liliana Benegas, (Maternidad Martín – Secretaría de Salud Pública – Municipalidad de Rosario, Rosario Santa Fe); Daniel Pryluka, Silvana Manganello (Hospital Velez Sarsfield, CABA), Rosana Costa, Mónica Moyano, (Hospital Evita Pueblo De Berazategui, Buenos Aires), Jonathan Zintgraff, Fabiana Garcia (Clínica Sagrado Corazón, CABA), Miriam Figueroa, Mariana Landa, German Bernardi, Angel Minguez (Hospital Misericordia Nuevo Siglo; Córdoba), Graciela Alicia Arriero, Damian Aguila (Hospital Roque Saenz Peña, Santa Fe), María Silvia Díaz, María Gabriela Mudrik (Hospital Materno Infantil San Roque, Entre Ríos), Nancy Veronica Panini, Alejandra Cuello (Policlinico Regional De Villa Mercedes, San Luis), Cristina Alicia Gonzalez, Erica Gerlach, Lein Hung Kuo (Hospital De Nivel III Obera, Misiones), Mónica Delfina Sparo, Jorge Hector Gentile, Claudia Henández (Hospital Municipal Ramon Santamarina, Buenos Aires), Adriana Margarita Ernst, Gabriela Ensinnck (Hospital De Niños V. J. Vilela, Santa Fe), Claudia María Alfonso, María Teresa Rodriguez Brieschke, Daniela D'Alessandro (Hospital Donacion F. Santojanni, CABA), María Silvana Vivaldo, Belen Malianni (Hospital De La Madre y El Niño, Formosa), Ana Berejnoi, Adriana Falco (Hospital Materno Infantil de Salta, Salta), María Ester Andriani, Silvana Fernandez (Hospital "Dr Julio Perrando", Chaco), Karina Contreras, Adriana Quiroga (Hospital de La Madre y El Niño de La Rioja, La Rioja), Graciela María Stafforini, María Cristina Aparicio (Hospital Artemides Zatti, Río Negro), Claudia Hernández, Claudia Sarkis (Hospital de Pediatría Prof. Dr. Juan P Garrahan, CABA), Rosana Pereda, Cecilia Echave (Hospital Pedro Elizalde, CABA), María Fernanda Arrieta, Daniela Musa (Centro De Microbiología Medica, Tucumán), Ana Maria Zaloff Dakoff, Teresa Alicia Corallo (Hospital Pediatrico Avelino Lorenzo Castelan, Chaco). This work was presented in part at the 28th ECCMID European Congress of Clinical Microbiology and Infectious Diseases, 2018 (Madrid, Spain).

This work was presented in part at the 28th ECCMID European Congress of Clinical Microbiology and Infectious Diseases, 2018 (Madrid, Spain).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2023.e22610>.

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Supplementary Figure S1

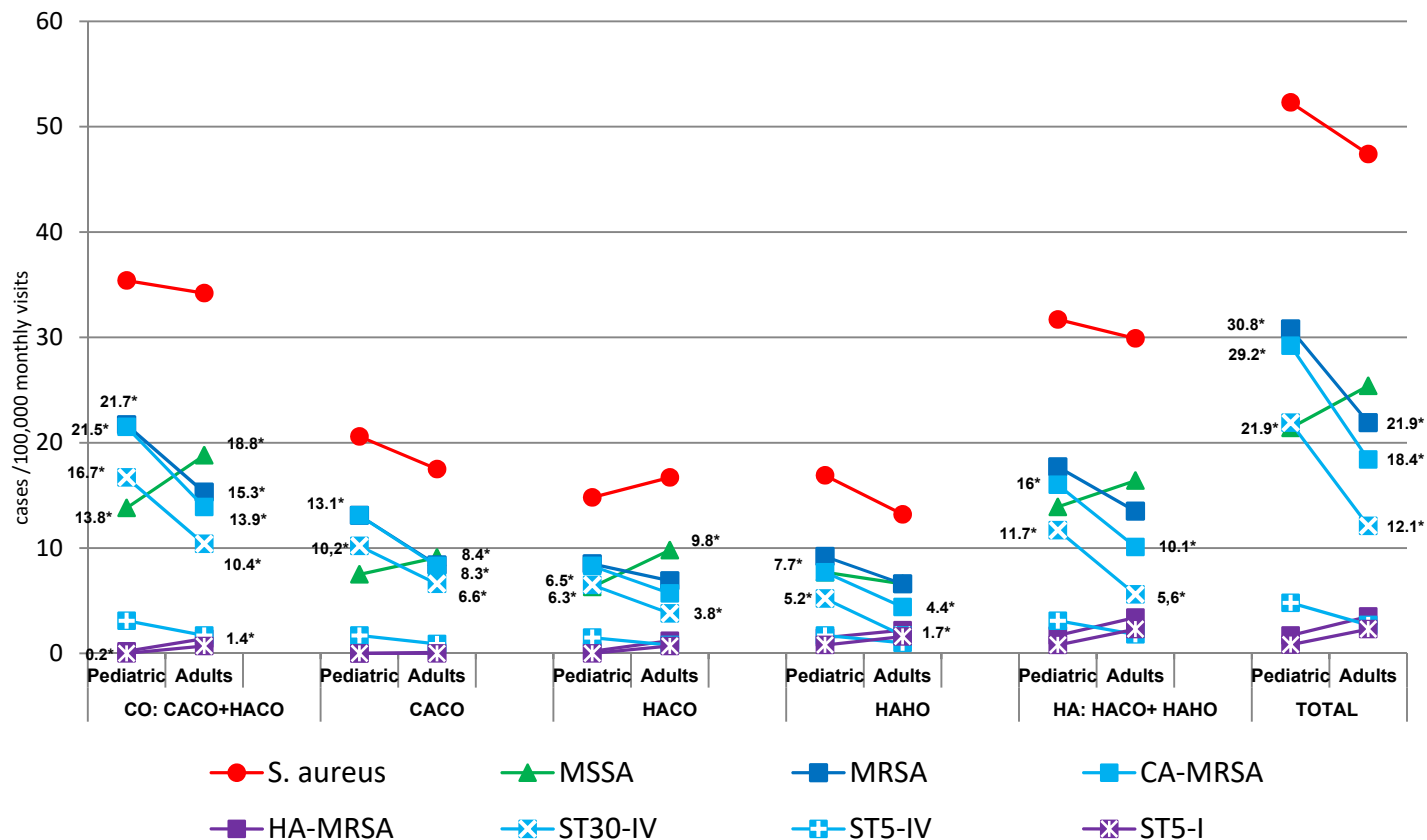


Figure SS1: Incidence of total infections caused by *S. aureus* (SA), MSSA, MRSA and MRSA genotypes (including CA-MRSAG and HA-MRSAG and major MRSA clones) in pediatric and adults by epidemiological criteria (CDC), April 2015, Argentina

Incidence: Number of cases /100,000 monthly visits. Number of visits (V): include outpatient facility, emergency service and admissions during one month.

n* : $P < 0.05$ by χ^2 test for the comparison of infections cases incidence between pediatric and adult patients.

Supplementary Figure S2

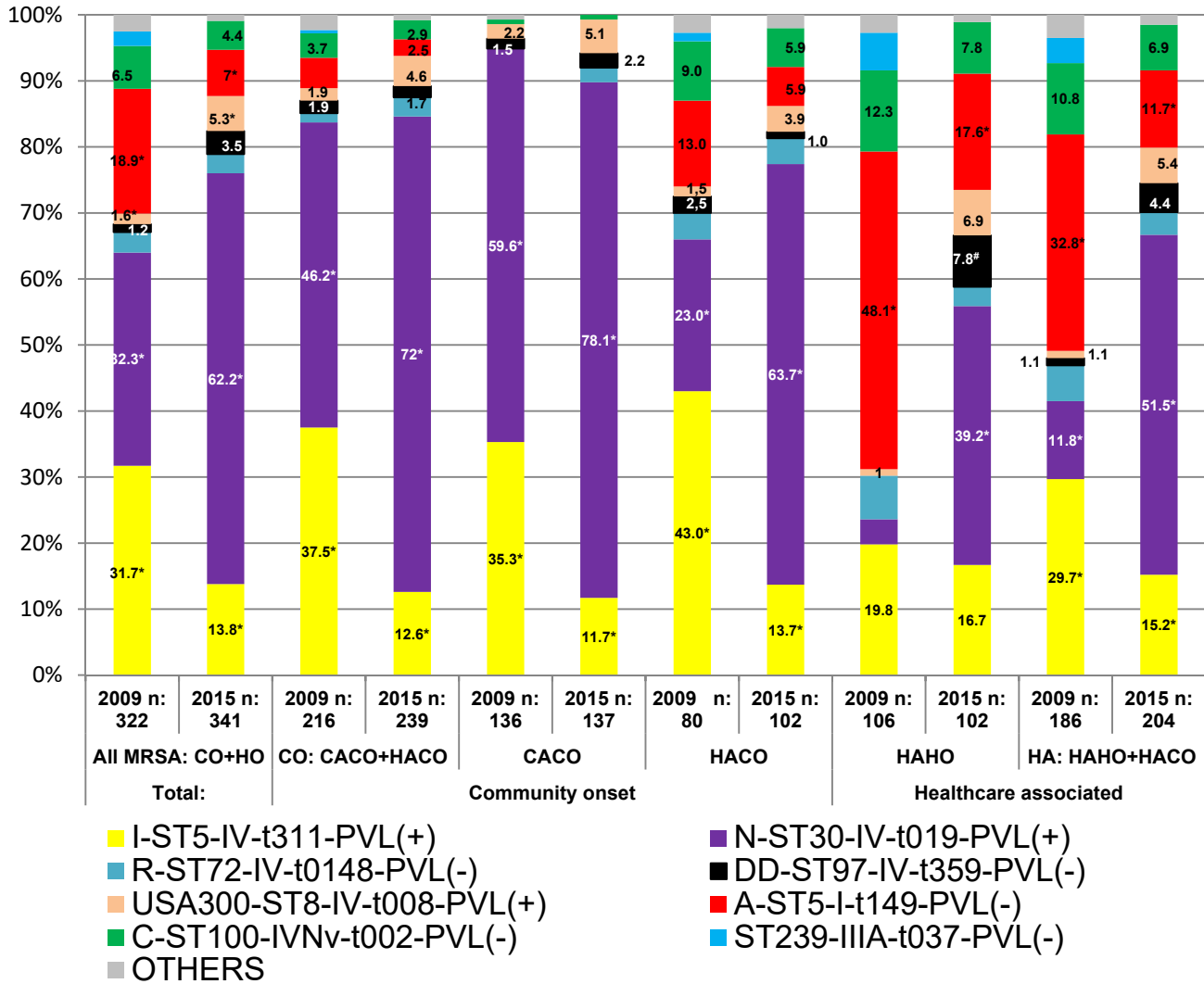


Figure SS2 : Relative proportions of major MRSA clones by epidemiological criteria and onset type of infection in entire population, 2009 and 2015, Argentina.

- $*P < 0.05$ by χ^2 test, for comparison of proportions of MRSA clone between 2009 and 2015.
- # ST97 Genotype detected for the first time causing HAHO infections
- Genotypes are denoted as: type (by PFGE)-Sequence Type (ST by MLST)-SCCmec type-*spa* type-presence (+) or absence (-) of PVL.
- CACO: community-associated community-onset infections, HA: healthcare-associated infections: including HACO: healthcare-associated community-onset and HAHO: healthcare-associated hospital-onset infections

Supplementary Figure S3

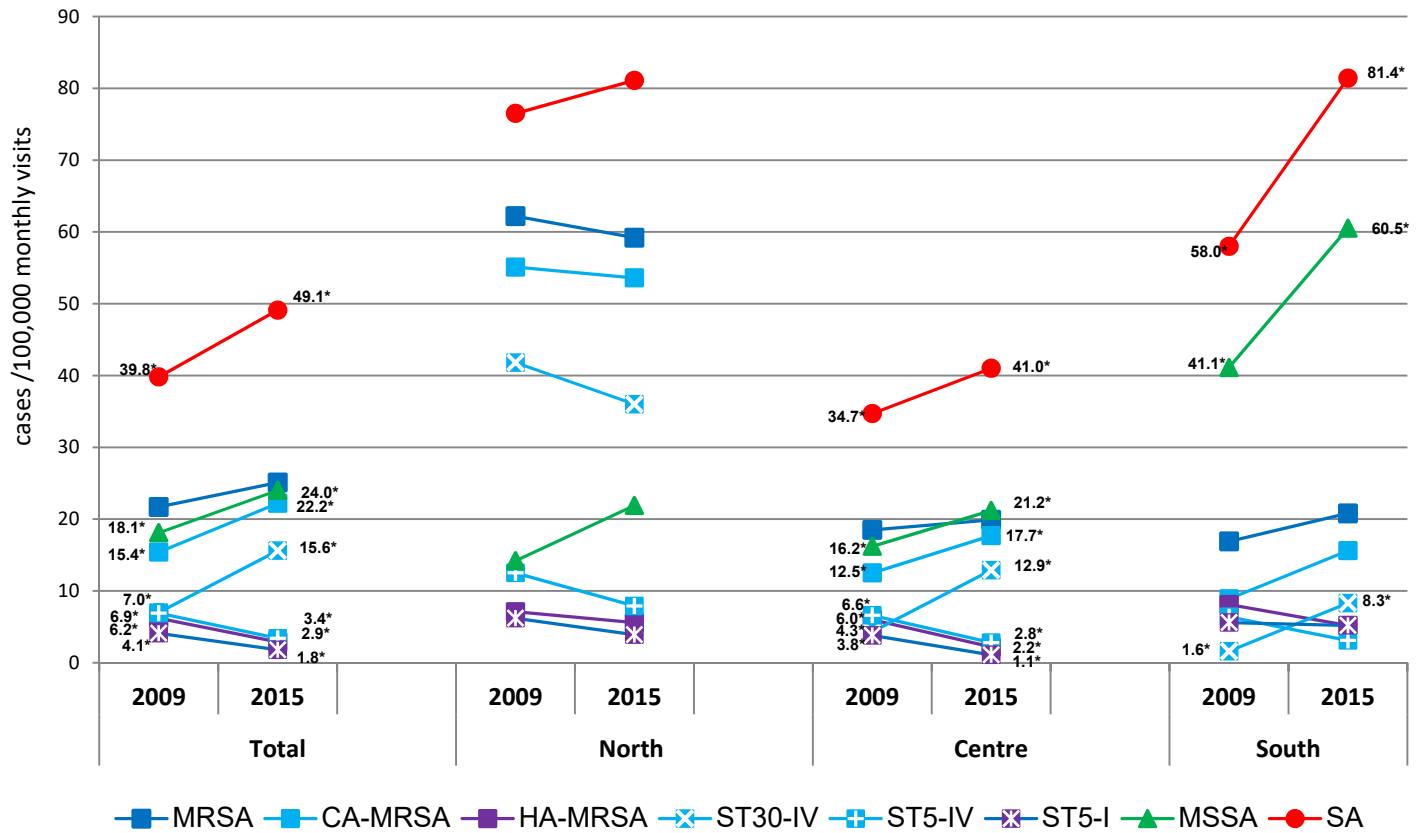


Figure SS3 Incidence of infections caused by *S. aureus* (SA), MRSA, and MRSA genotypes (including CA-MRSA_G and HA-MRSA_G and major MRSA clones) by regions of Argentina, between 2009 and 2015.

Incidence: Number of cases /100,000 monthly visits.

Number of visits (V): include outpatient facility, emergency service and admissions during that month.

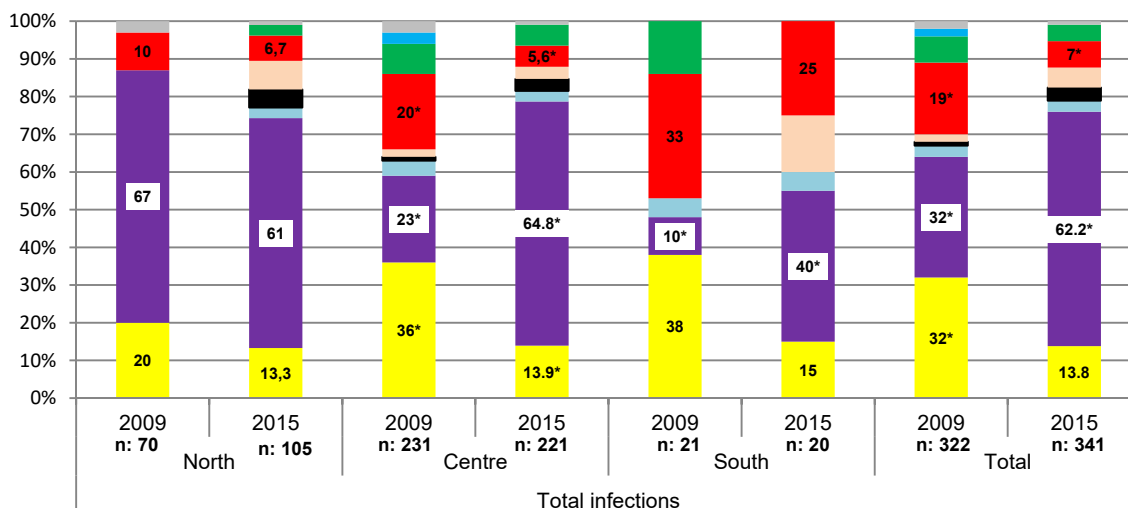
V₂₀₀₉: Total: 1,484,505; North: 112,427; Centre: 1,247,957 and South 124,121 visits

V₂₀₁₅: Total: 1,360,252 ; North: 177,554; Centre: 1,086,859 and South 95,839 visits.

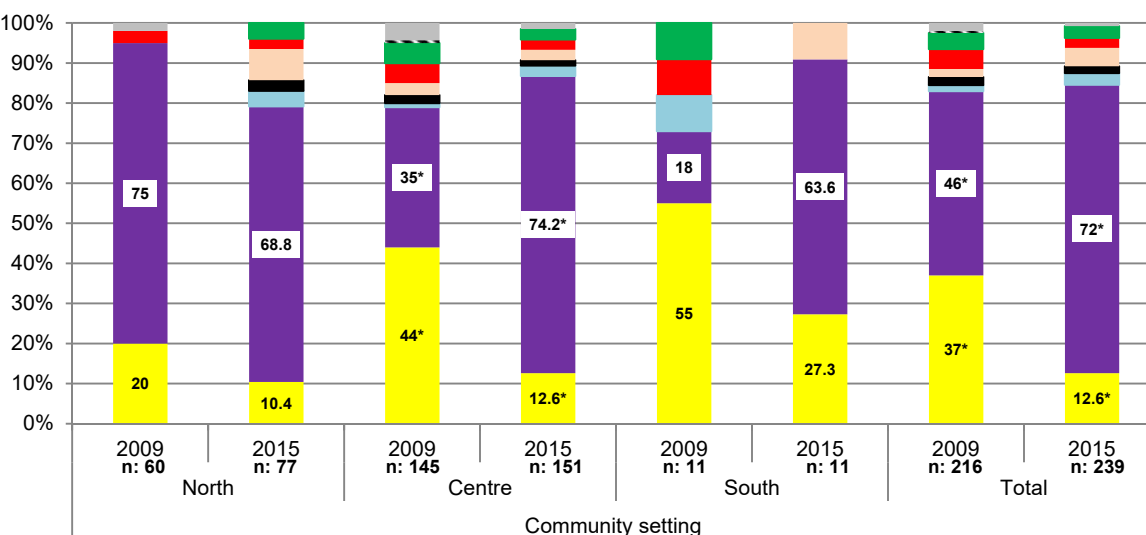
n*: $P < 0.05$ by χ^2 test for the comparison between 2009 and 2015 of the infections rates by regions of Argentina.

Supplementary Figure S4

A1.



A2.



A3.

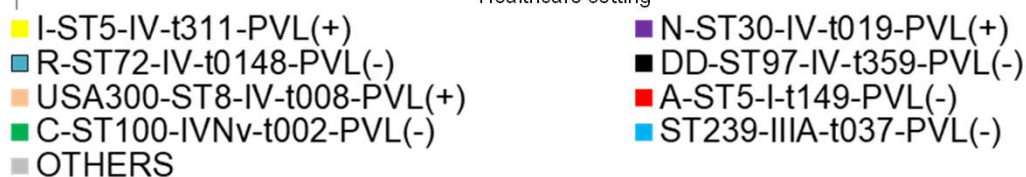
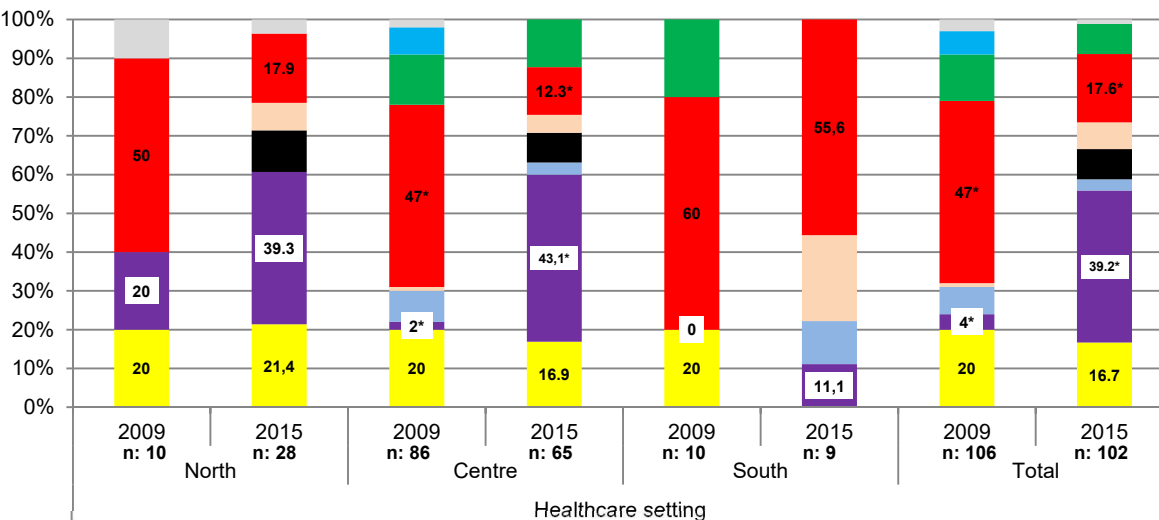


Figure S4. Distribution of MRSA clones by regions of Argentina: North, Centre and South, in (A1) total MRSA infections and both, (A2) community and (A3) healthcare setting, in 2009 and 2015, Argentina.

- $*P < 0.05$ by χ^2 test, for comparison of MRSA proportions caused by each genotype 2009 vs. 2015, both in the hospital and community settings.
- Genotypes are denoted as: type (by PFGE)-Sequence Type (ST by MLST)-SCC*mec* type-*spa* type-presence (+) or absence (-) of PVL.

Supplementary Table S1 Characteristics and incidence of *S. aureus*, MSSA and MRSA infections and location of 61 hospitals from 20 provinces and Buenos Aires city, by regions of Argentina (North, Centre and South), April 2015

Hospitals	Regions	Provinces	no. of beds	no. of admission	no. of visits ^a	<i>S aureus</i>		MSSA		MRSA	
						Number	Incidence ^b	Number	Incidence ^b	Number	Incidence ^b
1	North	Catamarca	100	343	2,781	2	72	1	36	1	36
2	North	Corrientes	159	509	5,293	4	75.6	0	0	4	75.6
3	North	Chaco	469	1933	21,752	18	82.8	3	13.9	15	68.9
4	North	Chaco	245	675	31,639	26	82.2	7	22.1	19	60.1
5	North	Chaco	77	537	14,914	10	67.1	1	6.7	9	60.4
6	North	Formosa	121	390	20,808	18	86.5	5	24	13	62.5
7	North	Formosa	128	329	3,800	3	78.9	1	26.3	2	52.6
8	North	Jujuy	110	472	5,970	5	83.7	1	16.7	4	67
9	North	La Rioja	226	940	5,878	5	85.1	1	17	4	68.1
10	North	La Rioja	176	474	10,130	9	88.8	7	69.1	2	19.7
11	North	Misiones	178	890	10,048	8	79.6	3	29.9	5	49.7
12	North	Salta	367	3324	15,457	14	90.6	5	32.3	9	58.3
13	North	Salta	223	1091	12,353	10	81	1	8.1	9	72.9
14 ^c	North	Tucumán	0	0	8,895	6	67.5	2	22.5	4	45.0
15	North	Tucumán	110	546	7,836	6	76.6	1	12.8	5	63.8
Total North			2,529	12,453	177,554	144	81.1	39	22.0	105	59.1
							range:		range:		range:
							67.1-88.8		0.0-69.1		36.0-75.6
16	Centre	Autonomous city of Buenos Aires	140	855	57,362	26	45.3	18	31.4	8	13.9
17	Centre	Buenos Aires	254	2,070	8,327	3	36	1	12	2	24
18	Centre	Autonomous city of Buenos Aires	81	369	5,474	2	36.6	1	18.3	1	18.3
19	Centre	Autonomous city of Buenos Aires	250	1,181	27,658	10	36.1	6	21.6	4	14.5
20	Centre	Autonomous city of Buenos Aires	300	917	49,959	21	42	12	24	9	18
21	Centre	Autonomous city of Buenos Aires	198	1,173	61,908	29	46.9	18	29.1	11	17.8
22	Centre	Buenos Aires	218	645	23,136	11	47.6	3	13	8	34.6
23	Centre	Buenos Aires	350	760	38,632	15	38.8	5	12.9	10	25.9
24	Centre	Buenos Aires	484	1,350	57,181	19	33.2	8	14	11	19.2
25	Centre	Buenos Aires	249	1,168	57,959	27	46.6	8	13.8	19	32.8
26	Centre	Buenos Aires	210	1,062	58,363	19	32.6	6	10.3	13	22.3
27	Centre	Autonomous city of Buenos Aires	110	453	8,839	3	34	1	11.3	2	22.7
28	Centre	Buenos Aires	168	375	5,593	2	35.8	1	17.9	1	17.9
29	Centre	Buenos Aires	245	816	21,536	9	41.7	4	18.6	5	23.2
30	Centre	Autonomous city of Buenos Aires	380	1,003	40,343	15	37.2	10	24.8	5	12.4
31	Centre	Buenos Aires	244	777	18,045	8	44.3	1	5.5	7	38.8
32	Centre	Autonomous city of Buenos Aires	513	2,049	50,487	21	41.6	9	17.8	12	23.8
33	Centre	Buenos Aires	100	498	14,833	7	47.2	3	20.2	4	27
34	Centre	Autonomous city of Buenos Aires	283	901	31,275	12	38.4	4	12.8	8	25.6
35	Centre	Córdoba	107	719	27,597	13	47.1	8	29	5	18.1
36	Centre	Córdoba	107	313	20,260	8	39.5	5	24.7	3	14.8
37	Centre	Córdoba	140	914	20,785	9	43.3	6	28.9	3	14.3
38	Centre	Córdoba	171	349	28,384	12	42.3	9	31.7	3	10.6
39	Centre	Córdoba	70	136	19,261	9	46.7	7	36.3	2	10.4
40	Centre	Córdoba	39	158	13,341	5	37.5	2	15	3	22.5
41	Centre	Córdoba	240	712	13,225	5	37.8	4	30.2	1	7.6
42	Centre	Córdoba	59	178	9,608	4	41.6	2	20.8	2	20.8
43	Centre	Córdoba	67	216	22,690	10	44.1	6	26.4	4	17.7
44	Centre	Córdoba	76	196	16,787	7	41.7	4	23.8	3	17.9
45	Centre	Córdoba	186	631	32,008	14	43.7	10	31.2	4	12.5
46	Centre	Córdoba	84	833	12,208	4	32.8	3	24.6	1	8.2
47	Centre	Entre Ríos	180	757	2,887	1	34.6	0	0	1	34.6
48	Centre	Mendoza	268	1,324	19,138	8	41.8	7	36.6	1	5.2
49	Centre	San Luis	50	645	29,249	12	41	7	23.9	5	17.1
50	Centre	Santa Fe	170	1,250	41,257	17	41.2	9	21.8	8	19.4
51	Centre	Santa Fe	180	137	31,038	13	41.9	5	16.1	8	25.8
52	Centre	Santa Fe	104	563	18,375	7	38.1	2	10.9	5	27.2
53	Centre	Santa Fe	100	515	19,546	8	41	1	5.1	7	35.9
54	Centre	Santa Fe	79	524	31,236	12	38.4	9	28.8	3	9.6
55	Centre	La Pampa	164	646	15,819	7	44.2	4	25.3	3	18.9
56	Centre	Santa Fe	208	704	5,250	2	38	1	19	1	19
Total Centre			7626	30,842	1,086,859	446	41.1	230	21.2	216	19.9
							range:		range:		range:
							32.6-47.6		0-36.3		5.2-38.8

57	South	Neuquén	243	858	25,514	23	90.1	19	74.5	4	15.7
58	South	Río Negro	80	319	22,685	15	66.1	10	44.1	5	22
59	South	Santa Cruz	100	310	7,084	6	84.7	5	70.6	1	14.1
60	South	Santa Cruz	223	633	22,743	19	83.5	13	57.1	6	26.4
61	South	Tierra del Fuego	92	394	17,813	15	84.2	11	61.8	4	22.4
Total South							81.4		60.5		20.8
			738	2514	95,839	78	range: 66.1-90.1	58	range: 57.1-74.5	20	Range: 14.1-26.4
TOTAL			10,893	45,809	1,360,252	668	49.1 Range (32.6-90.1)	327	24.0 Range (0-74.5)	341	25.1 range: (5.2-75.6)

^a. Number of visits: include outpatient facility, emergency service and admissions during November, 2015.

^b Incidence: Number of cases /100,000 monthly visits

^c It only has outpatient facility

Supplementary Table S2 Comparison of demographic and clinical characteristics of patients infected with *Staphylococcus aureus*, MSSA, MRSA and MRSA genotypes (CA-MRSA_G and HA-MRSA_G), in 2015 and between 2009 and 2015, Argentina

	All patients			MSSA		MRSA		2015	CA-MRSA _G			HA-MRSA _G		2015			
	2009 N: 591	2015 N: 668	P value 2009 vs 2015	2009 N: 269	2015 N:327	P value 2009 vs 2015	2009 N: 322		2015 N:341	P value 2009 vs 2015	P value MSSA- vs MRSA	2009 N:229	2015 N:302		P value 2009 vs 2015	2009 N: 93	2015 N: 39
Patient age at time of infection, n(%)																	
<1 year	55(9.3)	63(9.4)	0.97	27(10.0)	45(13.8)	0.19	28(8.7)	18(5.3)	0.12	0.0003	23(10.0)	14(4.6)	0.02	5(5.4)	4(10.3)	0.52	0.26
1-18 years	170(28.8)	188(28.1)	0.83	71(26.4)	58(17.7)	0.01	99(30.7)	130(38.1)	0.06	<0.0001	92(40.2)	126(41.7)	0.79	7(7.5)	4(10.3)	0.85	0.0003
19-30 years	66(11.2)	105(15.7)	0.02	23(8.6)	35(10.7)	0.47	43(13.4)	70(20.5)	0.02	0.0007	35(15.3)	64(21.2)	0.10	8(8.6)	6(15.4)	0.39	0.53
>30 years	300(50.8)	312(46.7)	0.16	148(55.0)	189(57.8)	0.54	152(47.2)	123(36.1)	0.0048	<0.0001	79(34.5)	98(32.5)	0.69	73(78.5)	25(64.1)	0.13	0.0002
Sex																	
Female, n(%)	250(42.3)	274(41.0)	0.68	116(43.1)	135(41.3)	0.72	134(41.6)	139(40.8)	0.89	0.96	96(41.9)	121(40.1)	0.74	38(40.9)	18(46.2)	0.71	0.57
Infection type^a	no:783 (%)	no:817 (%)		no:360 (%)	no:401 (%)		no:423 (%)	no:416 (%)			no:287 (%)	no:369 (%)		no:136 (%)	no: 47 (%)		
	[no]: 202	[no]: 176		[no]: 101	[no]: 98		[no]: 101	[no]: 78			[no]: 58	[no]: 66		[no]: 43	[no]: 12		
Skin and soft-tissue (SSTI)^b	270 (34.5)	338 (41.4)	0.0053	104 (28.9)	127 (31.9)	0.41	166 (39.2)	211 (50.7)	0.0010	<0.0001	158 (55.1)	206 (55.8)	0.76	8 (5.9)	5 (10.6)	0.32	<0.0001
	[2]	[0]					[2]				[2]						
SSTI uncomplicated	235 (30.0)	282 (34.5)	0.06	89 (24.7)	108 (26.9)	0.54	146 (34.5)	174 (41.8)	0.07	<0.0001	140 (48.8)	171 (46.3)	0.58	6 (4.4)	3 (6.3)	0.69	<0.0001
Abscess and cellulites ^c	235	282		89	108		146	174			140	171		6	3		
SSTI complicated	35 (4.5)	56 (6.9)	0.05	15 (4.2)	19 (4.7)	0.87	20 (4.7)	37 (8.9)	0.0472	0.0252	18 (6.3)	35 (9.5)	0.18	2 (1.5)	2 (4.3)	0.57	0.41
with bacteremia and secondary infections	33	54		14	19		19	35			17	33		2	2		
Necrotizing Fasciitis	1	2		0	0		1	2			1	2		0	0		
	[1]	[1]			[0]			[1]				[1]					
Diabetic foot infection	1	0		1	0		0	0			0	0		0	0		
Surgical Site (SSI)	56 (7.2)	30 (3.7)	0.0029	29 (8.1)	13 (3.2)	0.0052	27 (6.4)	17 (4.1)	0.25	0.62	15 (5.2)	13 (3.5)	0.39	12 (8.8)	4 (8.5)	0.94	0.11
Musculoskeletal infection	61 (7.8)	67 (8.2)	0.84	25 (6.9)	43 (10.7)	0.09	36 (8.5)	24 (5.8)	0.23	0.0154	23 (8.0)	23 (6.2)	0.45	13 (9.6)	1 (2.1)	0.09	0.34
	[21]			[10]			[11]				[9]			[2]			
Osteomyelitis	25	35		10	22		15	13			7	12		8	1		
Septic arthritis	17	13		7	8		10	5			9	5		1	0		
Prosthetic Joint infections	11	15		5	12		6	3			3	3		3	0		
Pyomyositis	5	4		2	1		3	3			3	3		0	0		
Spondylodiscitis	3	0		1	0		2	0			1	0		1	0		
Lower Respiratory tract infection^d	86 (10.9)	75 (9.2)	0.29	37 (10.3)	37 (9.2)	0.69	49 (11.5)	38 (9.1)	0.37	0.94	20 (6.9)	29 (7.9)	0.73	29 (21.3)	9 (19.1)	0.75	0.0177
Pneumonia	72	65		32	33		40	32			16	24		24	8		
Pleural abscess	14	10		5	4		9	6			4	5		5	1		
Upper respiratory tract infection	6 (0.77)	2 (0.24)	0.25	1 (0.27)	1 (0.25)	0.99	5 (1.2)	1 (0.29)	0.09	0.99	4 (1.4)	1 (0.27)	0.99	1 (0.73)	0	NA	
Acute middle Otitis	4	2		1	1		3	1			3	1		0	0		
Sinusitis	2	0		0	0		2	0			1	0		1	0		
Bacteremia^d	165 (21.1)	184 (22.5)	0.54	77 (21.4)	100 (24.9)	0.17	88 (20.8)	84 (20.2)	0.92	0.13	45 (15.7)	66 (17.9)	0.52	43 (31.6)	18 (38.3)	0.40	0.0010
	[130]	[129]		[64]	[67]		[66]	[62]			[33]	[51]		[33]	[11]		
Endocarditis	4 (0.51)	4 (0.48)	0.79	2 (0.56)	3 (0.83)	0.99	2 (0.62)	1 (0.29)	0.96	0.57	0	1		2 (1.5)	0		
	[1]	[3]		[0]	[3]		[1]	[0]			[0]	[0]		[1]	[0]		
Pericarditis	2 (<1)	0		1 (0.28)	0	NA	1 (0.31)	0	NA		1 (0.35)	0		0	0		
Catheter-associated infection	57 (7.3)	37 (4.5)	0.0229	31 (8.6)	23 (5.7)	0.16	26 (6.1)	14 (3.4)	0.14		7 (2.4)	8 (2.2)	0.82	19 (13.9)	6 (12.8)	0.83	0.0023
Deep abscess^e	11 (1.4)	15 (1.8)	0.66	8 (2.2)	6 (1.5)	0.46	3 (6.1)	9 (2.1)	0.0157	0.70	2 (0.69)	7 (1.9)	0.31	1 (0.73)	2 (4.3)	0.16	0.60
	[1]	[4]		[0]	[2]		[1]	[2]			[1]	[2]		[0]			
Lymphadenitis	4 (<1)	0		3 (0.83)	0	NA	1 (0.31)	0	NA		1 (0.35)	0	NA	0	0		
Central nervous system infection	18 (2.3)	3 (0.38)	0.0017	11 (3.1)	0	NA	7 (1.7)	3 (0.8)	0.55		6 (2.1)	2 (0.54)	0.09	1 (0.73)	1 (2.1)	0.99	0.30
	[7]			[4]			[3]				[2]			[1]			
Meningitis	13	3		9	0		4	3			3	2		1	1		
Cerebral ventriculitis	5	0		2	0		3	0			3	0		0	0		
Urinary tract infection	19 (2.4)	29 (3.5)	0.25	16 (4.4)	24 (6.0)	0.41	3 (0.31)	5 (1.2)	0.73	0.0004	1 (0.35)	5 (1.4)	0.23	2 (1.5)	0	NA	NA
	[19]	[29]		[16]	[24]		[3]	[5]			[1]	[5]		[2]	[0]		
Conjunctivitis	10 (1.3)	17 (2.1)	0.29	7 (1.9)	16 (4.0)	0.14	3 (0.31)	1 (0.29)	0.36	0.0006	2 (0.69)	0	NA	1 (0.73)	1 (2.1)	0.99	NA
Intra-abdominal infection	13 (1.7)	11 (1.6)	0.96	8 (2.2)	7 (1.7)	0.64	5 (1.2)	4 (1.2)	0.75	0.76	1 (0.35)	4 (1.0)	0.39	4 (2.9)	0	NA	NA
	[3]	[1]		[2]	[0]		[1]	[1]			[1]	[1]		[0]	[0]		
Dental adenophlegmon	1 (0.13)	0	NA	0	0		1 (0.31)	0	NA		1 (0.35)	0	NA	0	0		
Endometritis	0	1 (0.12)	NA	0	0		0	1 (0.29)	NA		0	1 (0.27)	NA	0	0		NA
Invasive Infection^f	296 (50.1)	363 (55.1)	0.09	143 (53.2)	201 (61.4)	P: 0.041 OR (95%CI): 1.4(1.01-1.95)	153 (47.5)	162 (47.5)	0.94	P: 0.0003/ OR (95%CI): 1.8 (1.30-2.40)	78 (34.1)	130 (43.0)	P: 0.0357/ OR (95%CI): 1.5 (1.03-2.09)	75 (80.6)	32 (82.1)	0.10	P: 0.0037/ OR (95%CI): 2.5 (1.33-4.65)

CA-MRSA_G and HA-MRSA_G community-associated and healthcare-associated methicillin-resistant *S. aureus* genotypes.

P values ≤ 0.05 for 2009 vs. 2015 comparison (for total *S. aureus*, MSSA, MRSA, CA-MRSA_G and HA-MRSA_G) and comparisons in 2015 (CA-MRSA_G vs HA-MRSA_G and MSSA vs MRSA) are shown in boldface font and underlined.

^aInfections are not mutually exclusive (783 infections in 591 patients in 2009 and 817 infections in 668 patients in 2015), values are number of infections and the percentages are indicated in parentheses.

[no]: numbers of patients with this secondary infections focus.

^bSSTI: Skin and Soft Tissue Infections: cases of primary skin infection were classified as uncomplicated, while complicated SSTI included cases with bacteremia secondary or it spreading to contiguous tissues.

^cAbscess and cellulites: in this category were also included: 3 cases of impetigo (1 from CA-MRSA_G and 2 from MSSA infections), 11 cases of folliculitis (8 from CA-MRSA_G and 3 from MSSA infections) and 4 cases of wound infections from HA-MRSA_G infections] in 2009 and 15 cases of folliculitis (10 from CA-MRSA_G and 5 from MSSA infections) in 2015.

^dBacteremia included those classified as primary, secondary and not specified.

^eDeep abscess included: *i*) 2009: breast (3 cases from MSSA infections), psoas (1 from CA-MRSA_G and 2 from MSSA infections), chest (1 from CA-MRSA_G), liver (1 from HA-MRSA_G), corneal, subphrenic and intra-abdominal (1 case each one from MSSA) abscesses, *ii*) 2015: psoas (4 cases from CA-MRSA_G and 3 from MSSA infections), liver (2 from CA-MRSA_G and 1 from HA-MRSA_G), spinal (1 from CA-MRSA_G and 1 from MSSA infections), retroperitoneal (2 from MSSA infections) and bladder (1 from HA-MRSA_G infections) abscesses

^fValues are number of patients and the percentages are indicated in parentheses. In 2009: Total: 591 patients: 269, 322 (229 and 93) with MSSA, MRSA (CA-MRSA_G and HA-MRSA_G) infections respectively, in 2015: Total: 668 patients: 327, 341 (302 and 39) with MSSA, MRSA (CA-MRSA_G and HA-MRSA_G) infections respectively.

CA-MRSA_G and HA-MRSA_G community-associated and healthcare-associated methicillin-resistant *S. aureus* genotypes.

% (n) of cases and % (n) of INV isolates, NA: Not applicable

^aN: A) Total number of patients and B) number of patients categorized by age group (pediatrics and adults) with community or healthcare associated *S. aureus* infections.

^bINV: A) Total number of patients and B) number of patients categorized by age group (pediatrics and adults) with community or healthcare associated *S. aureus* invasive infections.

^cIn: Incidence: Number of cases /100,000 monthly visits. Number of visits (V): include outpatient facility, emergency service and admissions during that month.

^dInI: Incidence of invasive infections: Number of cases of invasive infections/100,000 monthly visits. Number of visits (V): include outpatient facility, emergency service and admissions during that month

^eGenotypes (major clones) are denoted as: type (by PFGE)-Sequence Type (ST by MLST)-SCC_{mec} type
P values ≤ 0.05 for all comparisons are shown in boldface font.

Supplementary Table SS4 Evolution diagram of incidence of total (TI) and invasive (INV) infections caused by *S. aureus* (SA), MSSA, MRSA, and MRSA-genotypes in Argentine Hospitals (2009-2015), analysis by onset type and epidemiological criteria in (A) total population, (B) pediatrics, and (C) adults..

A) Total population

Incidence 2009 vs. 2015	Total population		CO: CACO+HACO		CACO		HACO		HAHO		HA: HACO+HAHO	
	T	INV	T	INV	T	INV	T	INV	T	INV	T	INV
Infections type												
S. aureus (SA)	>	>	>	>	>	>	>	>	~	~	>	>
MSSA	>	>	>	>	>	>	>	>	~	~	>	>
MRSA	~	~	>	~	~	~	>	>	~	~	~	~
CA-MRSA _G	>	>	>	>	~	~	>	>	>	>	>	>
HA-MRSA _G	<	<	~	~	~	~	~	~	<	<	<	<
N-ST30-IV ^a	>	>	>	>	>	~	>	>	>	>	>	>
I-ST5-IV ^a	<	~	<	<	<	<	<	~	~	~	<	~
A-ST5-I ^a	<	<	~	~	~	~	~	~	<	<	<	<
C-ST100-IVNv ^a	~	~	~	~	~	~	~	~	~	~	~	~

B) Adult patients

Incidence 2009 vs. 2015	Total population		CO: CACO+HACO		CACO		HACO		HAHO		HA: HACO+HAHO	
	T	INV	T	INV	T	INV	T	INV	T	INV	T	INV
Infections type												
S. aureus (SA)	>	>	>	>	>	>	>	>	~	~	~	>
MSSA	>	>	>	>	>	~	>	>	~	~	>	>
MRSA	~	~	~	>	~	~	~	>	~	~	~	~
CA-MRSA _G	>	>	>	>	~	~	>	>	>	>	>	>
HA-MRSA _G	<	<	~	~	~	NA	~	~	<	<	<	<
N-ST30-IV ^a	>	>	>	>	~	>	>	>	>	>	>	>
I-ST5-IV ^a	~	~	<	~	~	~	~	~	~	~	~	~
A-ST5-I ^a	<	<	~	~	0	0	~	~	<	<	<	<
C-ST100-IVNv ^a	~	~	~	~	~	NA	~	~	~	~	~	~

C) Pediatric patients

Incidence 2009 vs. 2015	Total population		CO: CACO+HACO		CACO		HACO		HAHO		HA: HACO+HAHO	
	T	INV	T	INV	T	INV	T	INV	T	INV	T	INV
Infections type												
S. aureus (SA)	>	~	~	~	~	~	~	~	~	~	>	~
MSSA	~	~	~	~	~	>	~	~	~	~	~	~
MRSA	>	~	~	~	~	~	~	~	>	~	>	~
CA-MRSA _G	>	~	~	~	~	~	>	~	>	~	>	>
HA-MRSA _G	~	~	~	~	0	0	~	NA	~	~	~	~
N-ST30-IV ^a	>	>	>	~	>	~	>	>	>	>	>	>
I-ST5-IV ^a	<	<	<	<	<	<	<	~	~	~	<	~
A-ST5-I ^a	~	~	0	0	0	0	0	0	~	~	~	~
C-ST100-IVNv ^a	~	~	~	NA	0	0	~	NA	~	~	~	~

▶ **Black** Increasing or < **white** Decreasing trend, ~ **gray** no significant change ($P < 0.05$ by χ^2 test for comparison) of infections incidence between 2009 and 2015 caused by *S. aureus* (SA), MSSA, MRSA, CA-MRSAG, HA-MRSAG and major clones for each infections category (onset type of infections and epidemiological criteria infections) in total (A) and by age group (B, C).

▶ **dark gray** **emergence** and spread in hospital setting.

^aGenotypes are denoted as: type (by PFGE)-Sequence Type (ST by MLST)-SCCmec type

Supplementary Table S5 Antimicrobial resistance rates of (A) main MRSA clones and (B) MSSA, in all isolates and by onset type of infections in Argentina, 2009 vs. 2015

A.

	MRSA clones										
	CA-MRSA-ST5-IV			CA-MRSA-ST30-IV			HA-MRSA-ST5-I				
	2009 no. (%) n: 102	2015 no. (%) n: 47	<i>P</i> value 2009 vs.2015	2009 no. (%) n: 104	2015 no.(%) n: 212	<i>P</i> value 2009 vs.2015	2009 <i>P</i> value ST5 vs ST30	2015 <i>P</i> value ST5 vs ST30	2009 no. (%) n: 61	2015 no. (%) n: 24	<i>P</i> value 2009 vs.2015
GEN	7 (7.0)	5 (10.6)	0.67	12 (12.0)	24(11.4)	0.97	0.3247	0.89	60 (98.4)	21 (87.5)	0.12
CIP	2 (2.0)	1 (2.1)	0.56	0 (0)	7 (3.3)	NA	NA	0.90	58 (95.1)	23 (95.8)	0.58
CLI	25 (24.0)	11 (23.4)	0.89	8 (8.0)	6 (2.8)	0.07	0.0032	0.0002	59 (96.7)	24 (100)	0.97
CLi	25 (24.0)	8 (17.0)	0.45	7 (7.0)	3(1.4)	0.0213	0.0014	0.0010	0 (0.0)	0 (0.0)	NA
CLiC	0 (0.0)	3 (6.4)	NA	1 (1.0)	3 (1.4)	0.81	NA	0.24	59 (96.7)	24 (100)	0.91
ERY	29 (28.4)	12 (25.5)	0.86	12 (12.0)	6 (2.8)	0.0025	0.0057	0.0001	60 (98.4)	24 (100)	0.61
RIF	1 (1.0)	0 (0.0)	NA	2 (2.0)	1 (0.5)	0.51	0.9863	NA	12 (19.8)	1 (4.2)	0.14
SXT	0 (0.0)	0 (0.0)	NA	0(0.0)	0 (0.0)	NA	NA	NA	0 (0.0)	1 (4.2)	NA
MIN	0 (0.0)	0 (0.0)	NA	0 (0)	0 (0.0)	NA	NA	NA	0 (0.0)	0 (0.0)	NA

B.

	MSSA										
	2009 Total, no. (%) N: 269	2015 Total, no. (%) N: 327	Total <i>P</i> value 2009 vs.2015	2009 CO, no. (%) n:159	2015 CO, no. (%) n: 232	CO <i>P</i> value 2009 vs.2015	2009 HO, no. (%) n: 110	2015 HO, no.(%) n: 95	HO <i>P</i> value 2009 vs.2015	2009 <i>P</i> value CO vs. HO	2015 <i>P</i> value CO vs. HO
GEN	12 (4.5)	38 (11.6)	0.0017	7 (4.4)	29 (12.5)	0.0110	5 (4.5)	9 (9.5)	0.25	0.79	0.56
CIP	5 (1.9)	12 (3.7)	0.18	1 (0.6)	8 (3.4)	0.13	4 (3.6)	4 (4.2)	0.83	0.17	0.97
CLI	11 (4.1)	33 (10.1)	0.0053	6 (3.8)	27 (11.6)	0.0110	5 (4.5)	6 (6.3)	0.79	0.97	0.21
CLi	5 (1.9)	23 (7.0)	0.0030	2 (1.3)	19 (8.2)	0.0062	3 (2.7)	4 (4.2)	0.83	0.70	0.29
CLiC	6 (2.2)	10 (3.1)	0.53	4 (2.5)	8 (3.4)	0.83	2 (1.8)	2 (2.1)	0.72	0.96	0.78
ERY	20 (7.4)	46 (14.1)	0.0102	13 (8.2)	37 (15.9)	0.0238	7 (6.4)	9 (9.5)	0.40	0.75	0.18
RIF	3 (1.1)	4 (1.2)	0.78	3 (1.9)	3 (1.3)	0.95	0 (0)	1 (1.1)	NA	NA	0.68
SXT	1 (0.4)	1 (0.3)	0.64	1 (0.6)	1 (0.4)	0.64	0 (0)	0 (0)	NA	NA	NA
MIN	0 (0.0)	0 (0.0)		0 (0.0)	0 (0)		0 (0)	0 (0)		NA	

CA-MRSA_G and HA-MRSA_G community-associated and healthcare-associated methicillin-resistant *S. aureus* genotypes; CO and HO: community-onset and healthcare-onset infections. CLiC and CLi: constitutive and inducible resistance to macrolide, lincosamide and streptogramin B, respectively, NA: Not applicable

^a $P > 0.05$ by χ^2 test, for comparison between MSSA isolates from patients with CO infections and those from HO infections, in both periods (2009 and 2015).

Significant differences ($P < 0.05$) for each comparison between resistances (%) are shown in boldface font

Gentamicin (GEN), Erythromycin (ERY), Clindamycin (CLiC and CLi: constitutive and inducible resistance to macrolide, lincosamide and streptogramin B, respectively), Ciprofloxacin (CIP), Rifampin (RIF), Trimethoprim/Sulfamethoxazole (SXT), Minocycline (MIN),

Supplementary Table 6: MSSA erythromycin-resistant isolates from both studies (2009 and 2015): proportions and genetic characteristics of each lineage, Argentina.

	2009, n: 20	2015, n: 46	Total: n: 66		
ST/CC/PFGE type	no/% ^a	no/% ^a	no/% ^a	RIDOM <i>spa</i> type: N.(%) ^b	Resistance to erythromycin Genotypes ^c : N.(%) ^b
8/8/USA300	4/20.0	15/32.6	19/28.8	t304: 12(63.1) (4) ^d , t024: 3(15.8), t190: 2(10.5), t648: 1, t682: (1) ^d	<i>ermA</i> : 1 (7), <i>ermB</i> : 3(20), <i>ermC</i> : 7 (47), <i>ermC-msrA1</i> : 2(13), <i>msrA1</i> : 6(40)
398/398/ND		10/21.7 ^e	10/15.1	t1451: 7(70.0) (2) ^d , t1985: 1, t571: 1, t3625: (1) ^d	<i>ermT</i> : 5(50), <i>ermT-ermC</i> : 5(50),
30/30/N	4/20.0	6/13.0	10/15.1	t012: 7(70.0), t021: 2(20.0) (1) ^d , t018: 1,	<i>ermA</i> : 5 (50), <i>ermC</i> : 3(30), <i>ermC-msrA1</i> : 2 (20),
45/45/AA	4/20.0	3/6.5	7/10.6	t065: 4(57.1), t026: 2 (28.6), (1) ^d t671: 1	<i>ermB</i> : 3 (43), <i>ermC</i> : 1(14), <i>ermB-msrA1</i> : 3 (43),
5/5/I	4/20.0	2/4.3	6/9.1	t002: 5(83.3)(1) ^d , t311: 1,	<i>ermA</i> : 2 (33), <i>ermB</i> : 1(17), <i>msrA1</i> : 3 (50),
121/121/V	1/5.0	2/4.3	3/ 4.5	t645: 1, t1688: 1, t159: 1	<i>ermC</i> :3 (100)
15/15/CC		3/6.5	3/ 4.5	t084: 3 (100), (1) ^d	ND: 2(67), <i>ermA</i> : 1
25/25/DDB,	2/10.0		2/3.0	t078: 1, t227: 1	<i>ermC</i> : 1, <i>msrA1</i> : 1
188/1/TT		2/4.3	2/3.0	t189: 2(100), (1) ^d	<i>ermC</i> : 1, <i>ermC-ermA</i> : 1
88/88/BB	1/5.0		1/ 1.5	t186: 1 ^d ,	<i>msrA1</i> : 1
97/97/DD		1/2.2	1/ 1.5	t2734: 1	ND: 1
10/10/NN		1/2.2	1/ 1.5	t414: 1	<i>ermB</i> : 1
6/5/JJ		1/2.2	1/ 1.5	t701: 1	<i>ermA</i> : 1

CC, Clonal Complex; ST, Sequence Type, PFGE type:Pulsed Field Gel Electrophoresis type; RIDOM *spa* type: staphylococcal protein A (*spa*) type assigned through the RIDOM databases (<http://spaserver.ridom.de>); the *spa* type was used to predict sequence types (STs). MLST was carried out in at least one strain of each *spa*-type detected, <https://pubmlst.org/organisms/staphylococcus-aureus> database,

^a no. (%), number and % of total MSSA from each year

^b N (%) number and % of each genotype (CC/ST/PFGE type)

^c The *ermA*, *ermB*, *ermC* and *msrA1* genes related to erythromycin resistance phenotype were analyzed and those detected are indicated. ND: undigested in PFGE.

^d Resistance to gentamicin in addition to the erythromycin resistance

^e All CC398-MSSA isolates (n: 10) were negative for *pvl* genes and positive for IEC system (IEC types: C, n: 6 and B, n: 4)