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# EXTRA-HOSPITAL STAY AND DIRECT COSTS CAUSED BY MULTIDRUG RESISTANT HEALTHCARE ACQUIRED INFECTIONS

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**Background** Healthcare acquired infections (HAI) are a recognized important cause of morbidity, mortality and economic burden which is divided into direct and indirect costs. Therefore we decided to carry out a case-control (1:1) matched study to estimate extra hospital stay in patients with infections caused by "Alert organisms" (mostly multidrug resistant) and economic burden in a teaching hospital in Rome.

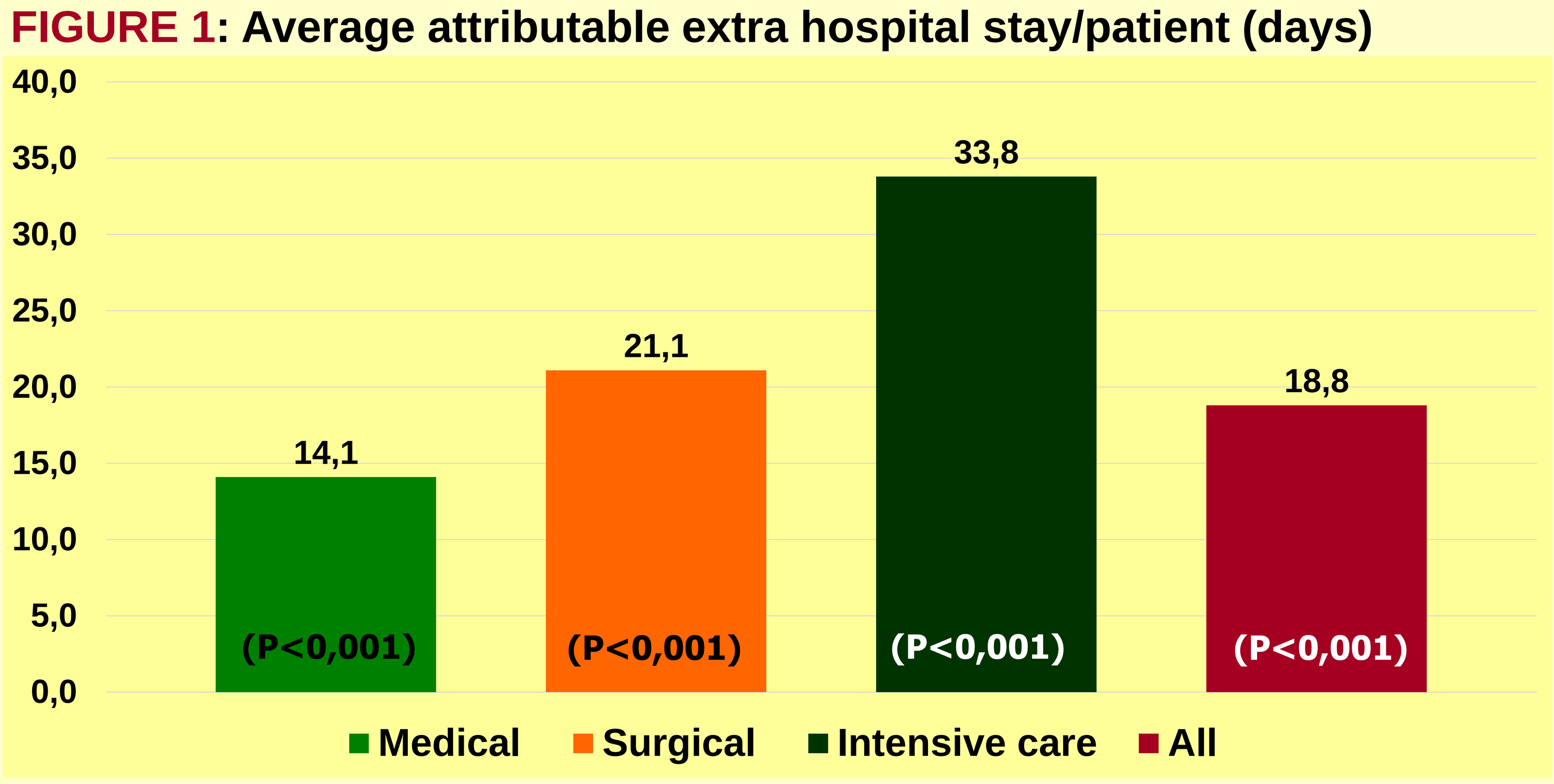
**Methods** The study was carried out in the 450 bed Teaching Hospital "Sant'Andrea" in Rome, from April to December 2015 all patients with infections caused by "Alert organisms" occurring > 48 hours after hospital admission were included in the study. In accordance with CDC definitions, the following Alert-HAI were included in the study: MRSA; VRE; MDR-*A. baumannii*; MDR-*P. aeruginosa*; Carbapenem resistant Enterobacteriaceae; *Clostridium difficile*. In cases and controls, the days of hospital stay were not always normally distributed. Consequently, the elaboration of the reference ranges were carried out by non-parametric methods. Therefore, days of hospital stay in cases and controls were compared by the use of the Mann-Whitney test. Statistical significance was defined using p<0,05. Among microorganisms the multi-drug resistance (MDR) was defined according to the ECDC guidelines [1]. All patients with no evidence of HAI by an alert microorganism were eligible as controls. When cases had more than one episode of a HAI by an alert microorganism, only the first episode was considered. We selected controls in a stepwise fashion, according to 6 matching variables with a 25 point scoring system: a) primary diagnosis according to the International Classification of Diseases (ICD-9-CM) (5 points); b) length of stay in controls equal to the interval from admission to infection in cases ±20% (LOS ±20%) (5 points); c) same ward of admission (5 points); d) surgical procedure (4 points); e) age ±5 years (4 points); f) same sex (2 points). Hospital management estimated the "hotel" average daily cost in medical (€ 400), surgical (€ 600) and ICU (€ 1.000). The antibiotic cost per unit was based on the prices actually paid by the hospital, which were 50% of the industry prices.

**TABLE 1**: Case-control matching appropriateness score

| Pairs of patients | Appropriateness score | Points | Matching appropriateness |
|---|---|---|---|
| 58 (47.5%) | 25 | 1450 | 100% |
| 14 (11,5%) | 23 | 322 | 92% |
| 28 (22,9%) | 21 | 588 | 84% |
| 22 (18,1%) | 20 | 440 | 80% |
| 122 | 22.9 | 2,800 | 91.8% |

**Results** Overall 122 patients developed HAI by "Alert organisms", 43 *Clostridium difficile* infections, 24 lower respiratory tract infections, 16 surgical site infections, 14 bloodstream infections, 12 urinary tract infections, 5 upper respiratory tract infections and 8 other infections during the study period. Males outnumbered females (72 vs. 50), the mean age was 72.1 ± 14.3 years (median 74, range 20-97) and at the moment of infection diagnosis 74 (60.7%) patients were in a medical ward, 30 (24.6%) in a surgical ward and 18 (14.7%) in an intensive care unit. The isolated "Alert organisms" were *C. difficile* 43 (35.2%), MRSA 23 (18.8%), *K. pneumoniae* 23 (18.8%), *A. baumannii* 19 (15.6%), *P. aeruginosa* 9 (7.4%), and others 5 (4.2%). Matching was carried out for all 122 cases, therefore the study finally included 244 patients (122 cases vs. 122 controls). Using the point scoring system made it possible to evaluate the appropriateness of matching. The average score for controls was 22.9 (91.8% matching appropriateness), 58 (47.6%) controls fully matched cases on all criteria and matching appropriateness was never <80% (TABLE 1). The ward of admission criterion was satisfied by all 122 (100%) controls. All except three control patients (97.5%) met the surgery criterion. All but nine controls (92.5%) matched the criterion for LOS. One-hundred-twelve controls (91.8%) matched cases for sex. One-hundred-eleven controls (91.0%) matched cases for age criterion. Ninety-five controls (75.0%) matched the diagnosis of admission. Crude case fatality rate (CFR) was 32.8% (40/122) in cases, 10.7% (13/122) in controls. Therefore CFR attributable to Alert-HAI was 22.1%, the estimated risk ratio for death 3.1; 1.73 – 5.46 (p=0.0001). Risk of death among cases was higher in ICU (44.4%) than in surgical wards (33.3%) and medical wards (29.7%). The age of the patients who died ranged from 52 to 97 years (mean 76.8 ± 10.5).

**FIGURE 1**: Average attributable extra hospital stay/patient (days)




**Results** Overall hospital stay in cases was 5,315 days (range 4 to 157), whereas in control group 3,024 (range 3 to 189). Alert-HAI attributable extra stay was 2,291 days (mean 18.8, median 19.0). Extra stays were respectively 33.8 days in ICUs, 21.2 days in surgical wards and 14.1 days in medical wards (p<0.001) (FIGURE 1). Among the 82 survived cases the overall Alert-HAI attributable extra stay was 741 days (mean 13.4, median 18.5). Considering different types of infection a significant major extra stay was represented by bloodstream infections (52.5 days), followed by urinary tract infections (20.1 days), surgical site infections (20.0 days), lower respiratory tract infections (19.0 days), *C. difficile* infections 7.5 (p<0.01) (TABLE 2).

**TABLE 2**: Attributable extra hospital stay associated to type of infection

| Site | n° pairs | Cases | | Controls | | *p value** | Attributable extra hospital stay/case |
|---|---|---|---|---|---|---|---|
| | | Mean ± DS | Median | Mean ± DS | Median | | days |
| Bloodstream infection | 14 | 77.9 ± 43.1 | 64.5 | 25.4 ± 18.9 | 19 | <0.001 | 52.5 |
| Urinary tract infection | 12 | 38.6 ± 21.9 | 37 | 18.5 ± 14.2 | 14.5 | 0.01 | 20.1 |
| Lower respiratory tract | 24 | 52.2 ± 22.9 | 45.5 | 33.2 ± 18.6 | 26 | <0.001 | 19.0 |
| Upper respiratory tract | 5 | 31.8 ± 12.4 | 33 | 24.6 ± 19.9 | 19 | 0.34 | 7.2 |
| Surgical site | 16 | 49.0 ± 37.1 | 43.5 | 29.0 ± 44.0 | 17 | <0.01 | 20.0 |
| Ulcer | 4 | 36.0 ± 8.9 | 37 | 28.7 ± 14.9 | 30 | 0.55 | 7.3 |
| *C. difficile* | 43 | 27.3 ± 18.2 | 24 | 19.8 ± 17.8 | 13 | <0.01 | 7.5 |
| Other | 4 | 61.7 ± 22.1 | 65.5 | 24.5 ± 20.4 | 12 | 0.08 | 37.2 |
| Total | 122 | 43.6 ± 30.3 | 38 | 24.8 ± 23.1 | 19 | <0.001 | 18.8 |

**Results** We also stratified data according to the isolated alert-microorganism and found the highest extra stay for *P. aeruginosa* (34.0 days), followed by *K. pneumoniae* (32.6 days), *A. baumannii* (20.9 days), MRSA (18.0 days), and *C. difficile* (7.5 days) (FIGURE 2). Applying the single day hospital cost to the "Alert organisms" attributable excess length of stay, the overall excess expenditure was €11,549 per patient. ICU costs per case (€33,833) were almost three fold higher than for surgical wards (€12,740) and medical wards were the lowest (€5,649) (FIGURE 3). As the average Alert-organism related antibiotic costs accounted for €1,200 per case, the final direct extra cost was €12,749 per patient.

**FIGURE 2**: Attributable extra hospital stay associated to type of microrganism (days)

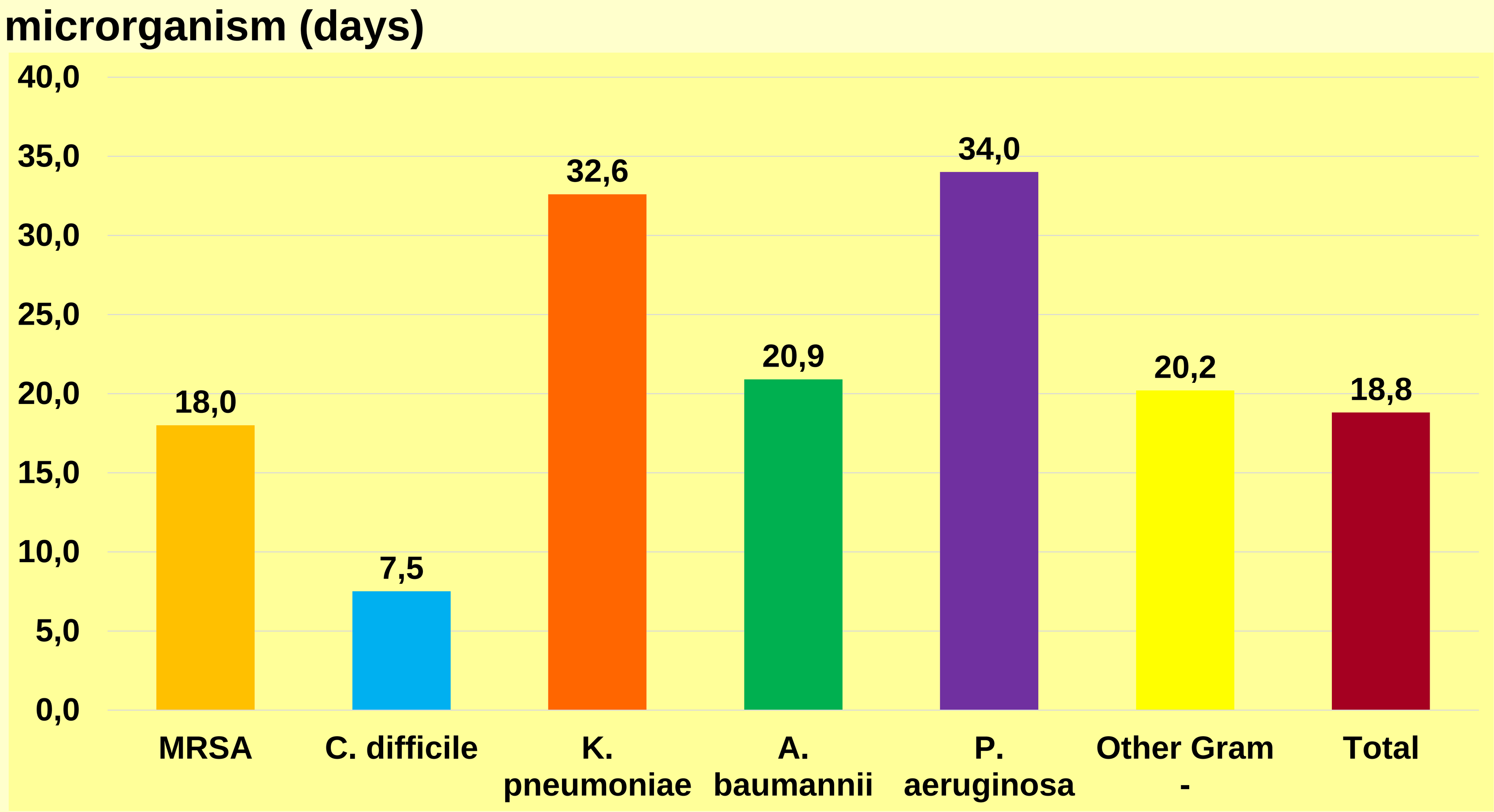
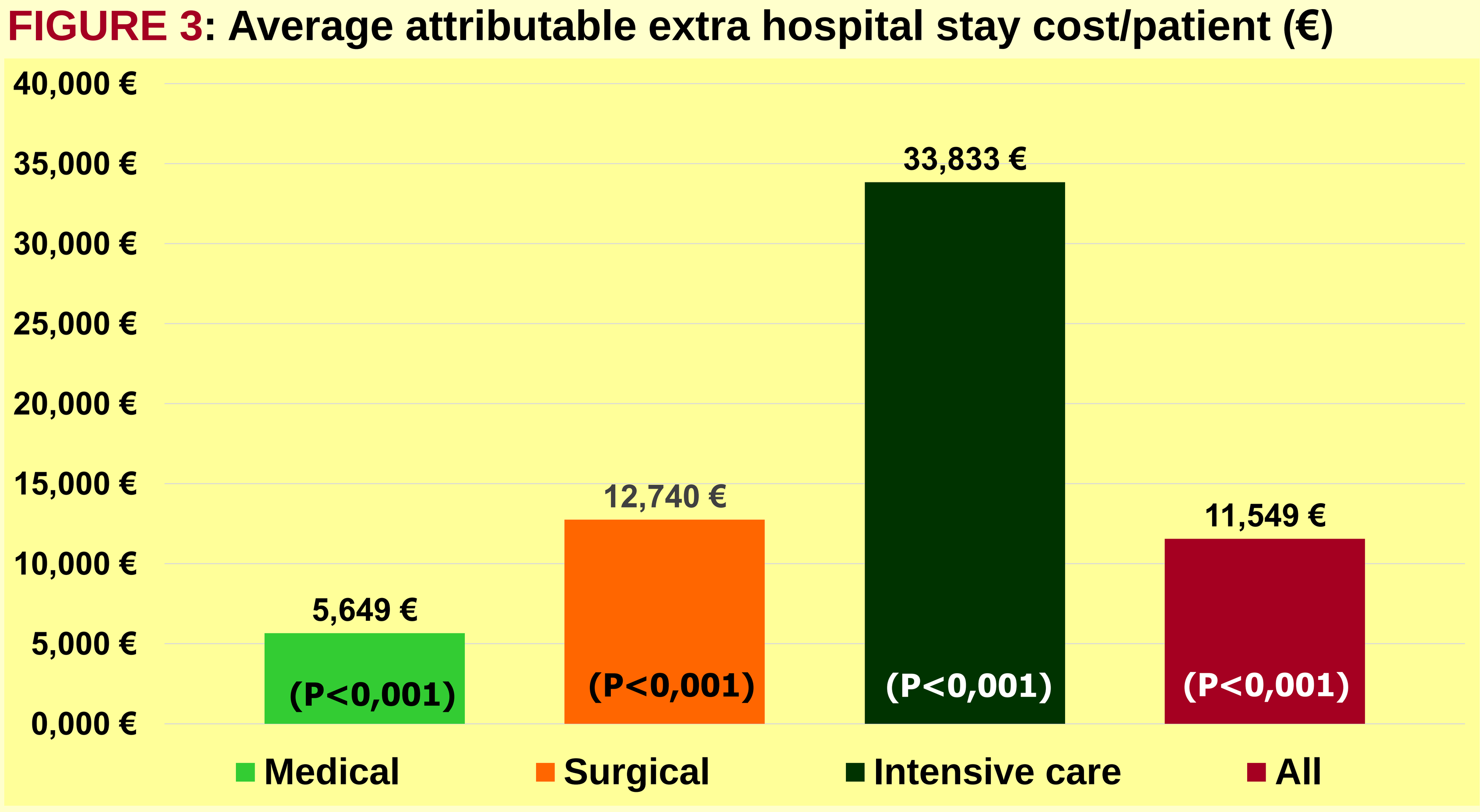



**FIGURE 3**: Average attributable extra hospital stay cost/patient (€)




**Conclusions** Extra-hospital stay and direct costs due to MDR-HAI were correctly estimated and resulted relevant. Economic evaluations may provide valuable information for decision making and could be useful in planning and justifying the resources needed in preventing multidrug resistant HAI. To this aim, an educational intervention for HAI prevention based on the Adult learning model was organized and implemented in our teaching hospital.

**References**

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