

Extensive clonal spread of *Klebsiella pneumoniae* ST11 NDM-1 in Poland

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Independence & disclosure information

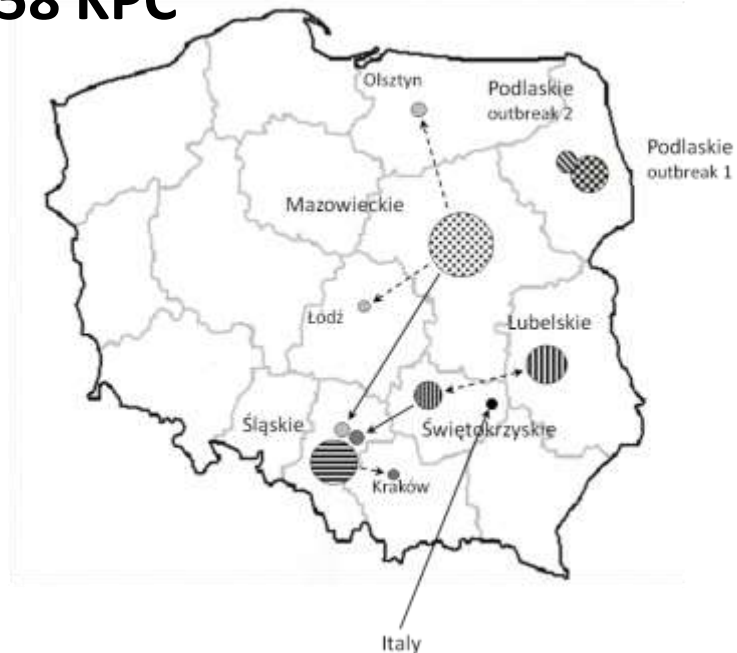
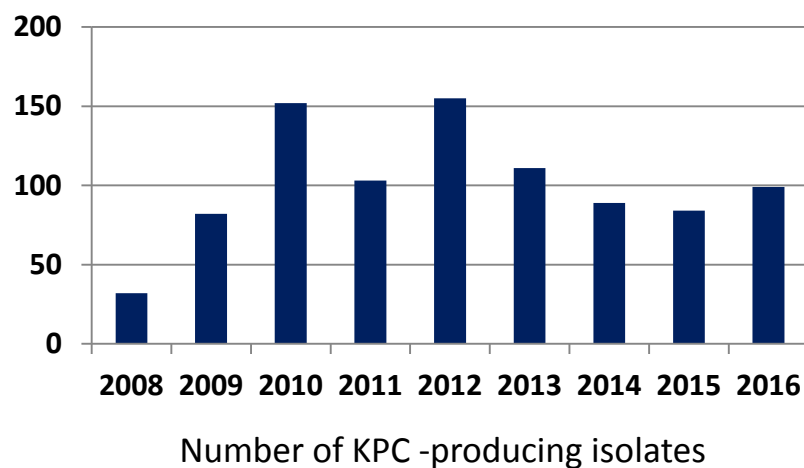
- Nothing to declare

CPE in Poland

- **Chronology of emergence:**
 - 2006: VIM (*K. pneumoniae*)
 - 2008: KPC (*K. pneumoniae*)
 - 2009: IMP (*Serratia marcescens*)
 - 2011: NDM (*Escherichia coli*)
 - 2012: OXA-48 (*Enterobacter cloacae*)

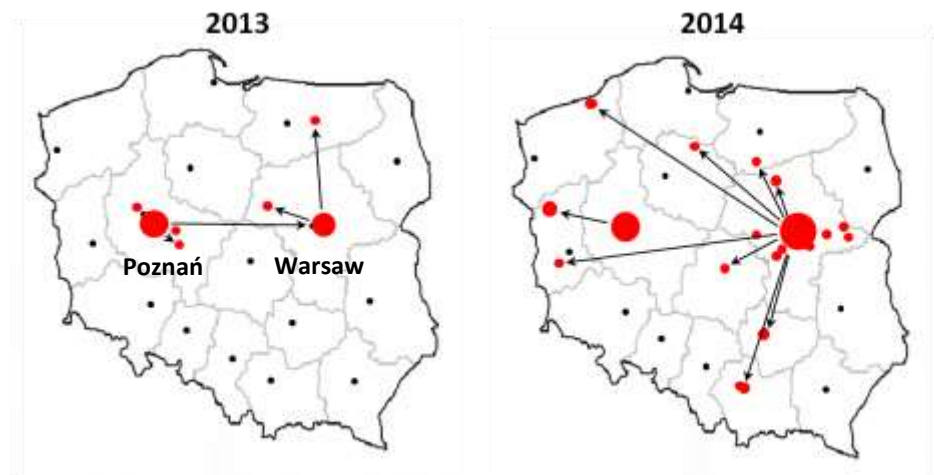
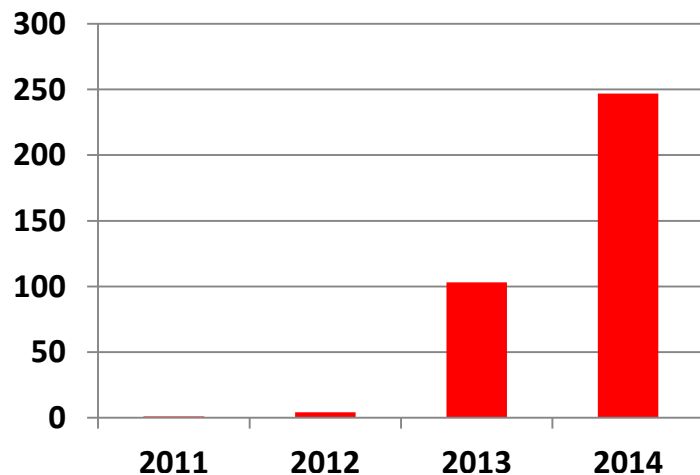
- **By the end of 2012: *K. pneumoniae* CG258 KPC**

6 major regional outbreaks:
- various CG258 genotypes



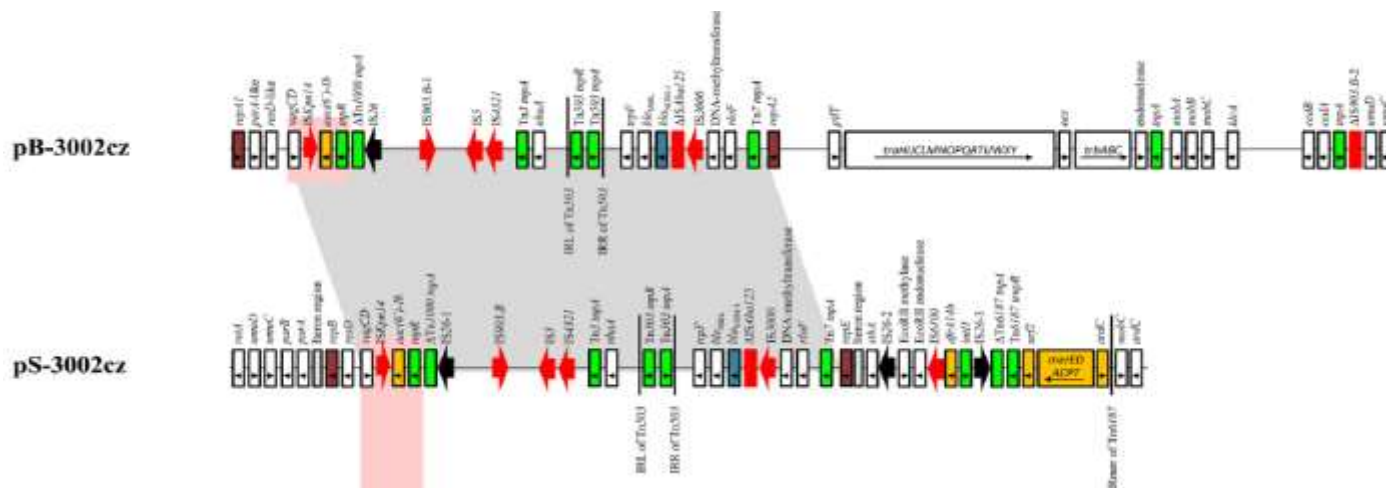
NDMs in Poland

- **2012-2014:**
 - **November 2012** - first *K. pneumoniae* NDM in Poznań, unknown origin
 - spread in the area of Poznań
 - **August 2013** – transmission of *K. pneumoniae* NDM from Poznań to Warsaw
 - spread in the area of Warsaw plus several further transfers
 - 4 documented imports from Montenegro, India and Afghanistan
 - **dramatic increase since 2013 – CPE problem No. 1 in antimicrobial resistance epidemiology**



NDM outbreak + imports, 2012-2014

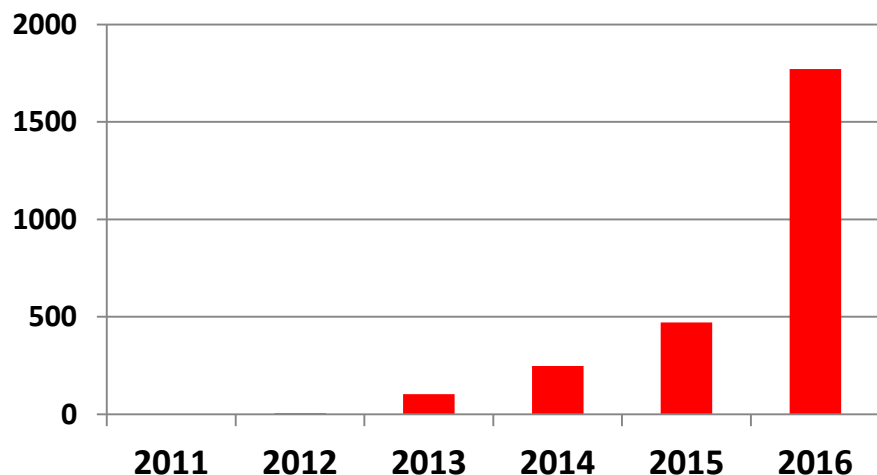
- **Molecular study:**
 - 66 representative *K. pneumoniae* isolates from 18 centres
 - plus 4 imports (*E. coli*, *K. oxytoca*, *K. pneumoniae*, *Proteus mirabilis*)
 - ***K. pneumoniae* ST11 subclone of high microheterogeneity**
 - varying in PFGE subtypes, plasmid profiles, plasmid rearrangements, β -lactamase content
 - similar to a Czech isolate from 2013 of Slovak origin in 2012
 - in 2015 similar NDM+VIM isolates in Greece
 - **two NDM-1-encoding plasmids** of low or no self-transmissibility potential
 - IncFII-like and IncR-like sharing a ~40-kb segment with the NDM-1 gene (Tn125 derivative)
 - often co-production of CTX-M-15



Baraniak et al. 2016;
 Studentova et al. 2015;
 Papagiannitsis et al. 2017

NDMs in Poland, 2015-2016

- **2015-2016:**
 - **further exponential increase in NDM cases, mostly *K. pneumoniae* (~99%)**
 - **1771 new cases in 2016; 142 hospitals, 17 LTCFs (~40% infected, ~60% colonized only)**
 - **many regions, predominantly in the Warsaw area (n=1394)**
 - **the situation in the Poznań area has been successfully controlled** since the mid-2014
 - **several documented imports of various species (e.g. India, DR Congo, Georgia)**
 - **the „Tunisian” import in March 2015 to Warsaw hospitals:**
 - victims of the terrorist attack in Tunis
 - at least 3 patients colonized with CPE, incl. *K. pneumoniae* ST147 NDM-1



RAPID COMMUNICATIONS

NDM-1- or OXA-48-producing Enterobacteriaceae colonising Polish tourists following a terrorist attack in Tunis, March 2015

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Izdebski et al. 2015

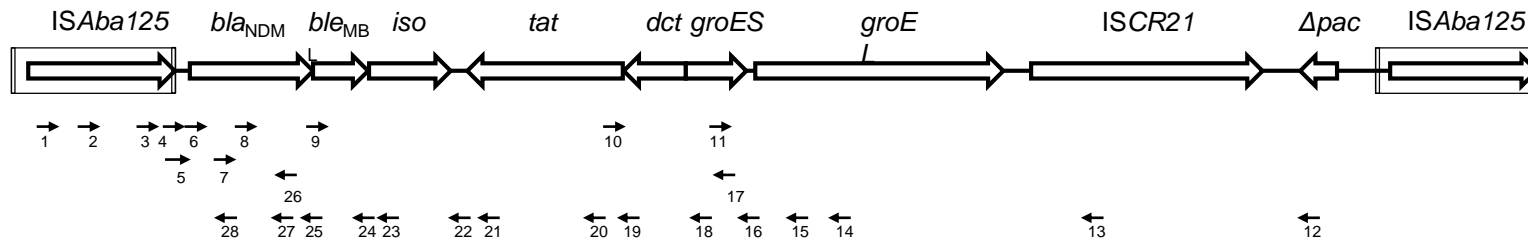
Objectives & methods

- **To assess how far the NDM increase in 2015-2016 was due to:**
 - continuation of the *K. pneumoniae* ST11 outbreak
 - possible new outbreaks following documented or non-documented imports
- **Study material:**
 - **all of the 1342 unique NDM isolates from 04.2015-08.2016** (1183 from the Warsaw area)
 - 1334 *K. pneumoniae*, 6 *E. coli*, 1 *K. oxytoca*, 1 *C. freundii*
 - from 113 hospitals from 13 administrative regions (69 from the Warsaw area)
- **Methods:**
 - NDM detection: Carba NP test and PCR – all isolates
 - typing screening: **polymorphism of Tn125-like elements** by PCR mapping – all isolates
 - **PFGE and MLST** – representatives of the „ST11 Tn125 type” and all isolates with „new” types
 - *bla*_{NDM} sequencing and plasmid profiling by the S1-hybridization for as above
 - β -lactamase profiling by PCR and sequencing for for as above

Tn125 elements in Poland: 2012-03.2015

- In *Enterobacteriaceae* the bla_{NDM} Tn125 transposon is usually truncated at random positions: **Tn125 derivatives as markers for the 1st line typing screening**
- **Polish NDM producers, 2012-03.2015:**
 - ~500 isolates of the *K. pneumoniae* ST11 outbreak with the **Tn125A type**
 - 3 *K. pneumoniae* ST147 isolates from Tunisia with the **Tn125B type**
 - 4 other documented-import isolates with **other Tn125 types**

Poirel et al. 2012
Toleman et al. 2012



Tn125A type *K. pneumoniae* ST11 plus *E. coli* ST10 & ST744 (outbreak 2012-2014)

Tn125B type *K. pneumoniae* ST147 (Tunisia 03.2015)

Other Tn125 types *E. coli* ST448 (India)

Other Tn125 types *P. mirabilis* (Afghanistan)

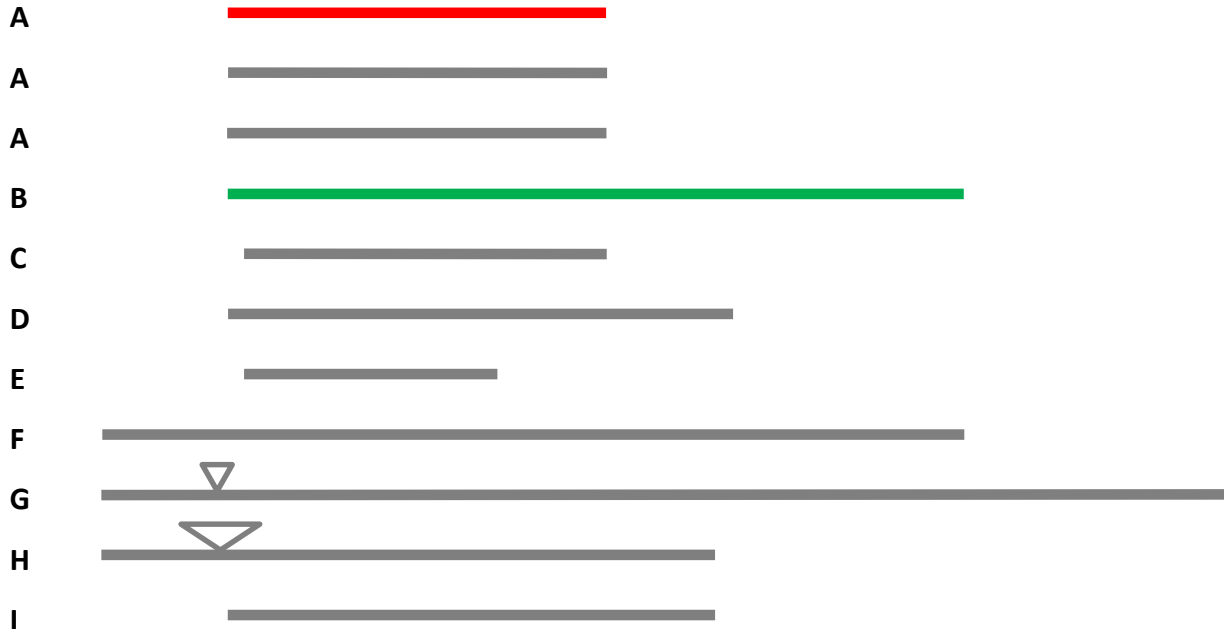
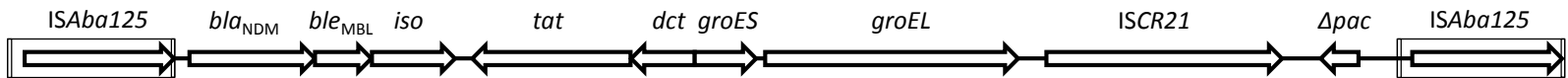
Other Tn125 types *K. pneumoniae* ST45 (???)

Other Tn125 types *K. oxytoca* ST146 (Montenegro)

Baraniak et al. 2016
Izdebski et al. 2015

Main results (1)

- **Tn125 elements in Poland: 03.2015-08.2016 – 9 different derivatives (A-I):**
 - 1326 isolates (~99%) with the **Tn125A type**
 - 7 isolates (~0,5%) with the **Tn125B type**
 - 9 isolates (~0,5%) with 7 new Tn125C-I types



Main results (2)

- Species – clones – NDM variants – NDM plasmids:

	n	species - clone	PFGE	NDM	NDM plasmids (kb)
Tn125A	214	<i>K. pneumoniae</i> ST11	A	NDM-1	~80-100
	4	<i>E. coli</i> ST101, ST224, new		NDM-1	~90; ~200; ?
	1	<i>K. oxytoca</i> ST88		NDM-1	~160
Tn125B	7	<i>K. pneumoniae</i> ST147	B1-2	NDM-1	~50+~130
Tn125C	2	<i>C. freundii</i> ST8; <i>E. coli</i> ST1196		NDM-1	~190; ?
Tn125D	1	<i>E. coli</i> STnew		NDM-5	~140
Tn125E	1	<i>E. coli</i> ST224		NDM-1	?
Tn125F	1	<i>K. pneumoniae</i> ST873		NDM-1	~180
Tn125G	1	<i>K. pneumoniae</i> ST147	B3	NDM-1	<50+~150
Tn125H	1	<i>K. pneumoniae</i> ST11	D	NDM-5	?
	1	<i>K. pneumoniae</i> ST11	F	NDM-1	~130
Tn125I	1	<i>K. pneumoniae</i> ST22		NDM-1	~130

Conclusions

- **NDM-producing *Enterobacteriaceae* in Poland:**
 - rapid increase since the end of 2012
 - **largely due to clonal spread of *K. pneumoniae* ST11 NDM-1:**
 - originally interregional Poznań – Warsaw
 - exports to other regions commence new hospital/regional outbreaks over the country
 - controlled in the area of Poznań due to coordinated regional effort (9 cases in 2016)
 - limited dispersal of the „Tunisian” *K. pneumoniae* ST147 NDM-1 (7 cases; 3 cities)
 - several new sporadic imports (documented or revealed by the molecular data)
- **unprecedented NDM outbreak in a non-endemic country observed in real-time**
- **large threat for public health in Poland**

Tn125	Species	MLST	PFGE	NDM	Plasmid <i>bla</i> _{NDM} (kb)	Other β -lactamases
A	<i>K. pneumoniae</i> (n=1321)	ST11	KpnA	1	ND	ND
	<i>E. coli</i> (n=1)	NEWST	EcoC	1	~210	CTX-M-15; TEM-1
	<i>E. coli</i> (n=2)	ST101	EcoD	?	~90	TEM-1
	<i>E. coli</i> (n=1)	ST224	EcoE	1	chromosome	CTX-M-15
	<i>K. oxytoca</i> (n=1)	ST88	KoxA	1	~160	CTX-M-3
B	<i>K. pneumoniae</i> (n=7)	ST147	KpnB (1-3)	1	~50, ~130	CTX-M-15; TEM-1
C	<i>C. freundii</i> (n=1)	ST8	CfrA	1	~190	CMY-116; TEM-1
	<i>E. coli</i> (n=1)	ST1196	EcoA	1	?	CMY-4; TEM-30
D	<i>E. coli</i> (n=1)	NEWST	EcoB	5	~140	CTX-M-15; TEM-1
E	<i>E. coli</i> (n=1)	ST224	?	1	?	CMY-4; TEM-1
F	<i>K. pneumoniae</i> (n=1)	ST873	KpnE	1	~180	CTX-M-15 ; TEM-1
G	<i>K. pneumoniae</i> (n=1)	ST147	KpnB2	1	<50; ~150	CMY-6
H	<i>K. pneumoniae</i> (n=1)	ST11	KpnF	1	~130	CTX-M-15; TEM-1
	<i>K. pneumoniae</i> (n=1)	ST11	KpnD	5	?	CTX-M-15; TEM-1
I	<i>K. pneumoniae</i> (n=1)	ST22	KpnC	1	~130	CTX-M-15; SHV-?; TEM-1