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1                    **Unusual initial abdominal presentations of invasive meningococcal disease**

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14                    **40-word summary**

15                    Early abdominal presentations of invasive meningococcal disease are increasingly  
16 reported. Our work increases the awareness of these forms by clinicians. Rapid management  
17 should reduce the high fatality rate that is associated with these presentations and avoid  
18 unjustified interventions (e.g. appendectomy).

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21                    **Running title:** Abdominal forms of meningococcal disease

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23

24 **Abstract**

25 **Background** Invasive meningococcal disease (IMD) is recognized as septicemia and/or  
26 meningitis. However, early symptoms may vary and are frequently nonspecific. Early  
27 abdominal presentations have been increasingly described. We aimed to explore a large  
28 cohort of patients with initial abdominal presentations for association with particular  
29 meningococcal strains.

30 **Methods** Confirmed IMD cases in France between 1991-2016 were screened for the presence  
31 within the 24 hours before diagnosis of at least one of the following criteria (1) abdominal  
32 pain, (2) gastro-enteritis with diarrhea and vomiting, (3) diarrhea only. Whole genome  
33 sequencing was performed on all cultured isolates.

34 **Results** We identified 105 cases (median age 19 years) of early abdominal presentations with  
35 a sharp increase since 2014. Early abdominal pain alone was the most frequent symptom  
36 (n=67, 64%), followed by gastro-enteritis (n=26, 25%) and diarrhea alone (n=12, 11%).  
37 Twenty patients (20%) had abdominal surgery. A higher case fatality rate (24%) was  
38 observed in these cases compared to 10.4% in all IMD in France (p=0.007) with high levels of  
39 inflammation markers in the blood. Isolates of group W were significantly more predominant  
40 in these cases compared to all IMD. Most of these isolates belonged to clonal complex ST-11  
41 (cc11) of the sublineages of the South American-UK strain.

42 **Conclusions** Abdominal presentations are frequently provoked by hyperinvasive isolates of  
43 meningococci. Delay in the management of these cases and the virulence of the isolates may  
44 explain the high fatality rate. Rapid recognition is a key element to improve their management.

45

46 **Key words:** Abdominal; Meningococcal disease; typing, serogroup; whole genome  
47 sequencing; clinical presentation

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## 50 **Introduction**

51 Invasive meningococcal disease (IMD) is an acute and severe infection caused by *Neisseria*  
52 *meningitidis* (Nm). It is a major cause of morbidity and mortality and is responsible for 1.2  
53 million cases of IMD and 135,000 deaths each year worldwide [1]. Invasive isolates of Nm  
54 are usually capsulated and they are classified into serogroups according to their capsular  
55 polysaccharides. Six serogroups (A, B, C, W, Y and X) are responsible virtually of all IMD  
56 worldwide but with variable geographical distribution [1, 2].

57 Moreover, invasive meningococcal isolates frequently belong to hyperinvasive lineages that  
58 were defined on the basis of molecular typing using multilocus sequence typing (MLST). This  
59 approach determines the sequence types (ST) using DNA sequences of 7 meningococcal loci.  
60 Close STs can be grouped into clonal complexes (cc) [3]. More recently, the next generation  
61 sequencing methods allowed more resolution through the analysis of whole genome  
62 sequencing (WGS) [4]. Interestingly, meningococcal hyperinvasive isolates of serogroup W  
63 (NmW) belonging to the cc11 were resolved into several strains on the basis of core genome  
64 MLST (cgMLST): the “Anglo-French-Hajj” strain and the “South American-UK” strain [5].  
65 The later strain was further shown to include two sublineages corresponding to the recent  
66 expansion of this strain in Europe: the original UK strain” and the “UK 2013-strain [5, 6].  
67 These strains and sublineages have been co-circulating in France [7].

68 IMD is usually notified as septicaemia and/or meningitis but other clinical forms are also  
69 observed such as septic arthritis, pericarditis and invasive pneumonia [8]. However, the early  
70 symptoms at the onset of the disease may vary in frequency and time of appearance.  
71 Thompson et al [9] related the frequency and time of onset of the clinical features of IMD in  
72 children and adolescents before admission to hospital. Non-specific symptoms and signs were  
73 reported to appear early such as leg pain that was reported in 20-50% of patients with a

74 median time of onset of 7 hours before admission. Diarrhea also was reported during the first  
75 24 hours (median time of onset of 9 hours before admission) but to a lesser extent (6.6%).  
76 Abdominal presentations were also rarely reported in a previous French study and accounted  
77 for 1% of all IMD cases between 1999 and 2002 [10]. In 2012, in Chile and among IMD  
78 cases due to isolates of serogroup W, diarrhea was the only symptom that was significantly  
79 ( $p=0.03$ ) over-represented among the fatal cases comparing with the survivors (56% vs 27%)  
80 [11]. More recently, Campbell et al reported that 7 out of 15 IMD cases (of whom 5 died)  
81 presented predominantly with a history of acute gastrointestinal symptoms in the 24  
82 hours before attending hospital. These cases were all provoked by the currently expanding  
83 hypervirulent capsular serogroup W strain (the South American UK strain and its sublineages)  
84 [12]. The link of these NmW isolates with abdominal presentations of IMD remains to be  
85 evaluated in large cohorts of patients. We therefore aimed in this work to review the database  
86 of the French National Reference Centre to describe a large cohort of patients with abdominal  
87 presentation of IMD in terms of clinical, biological and bacterial parameters. We also aimed  
88 to analyze the association of different genomic types of meningococci with abdominal  
89 presentations of IMD.

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## 100 **Methods**

### 101 **Ethics statement**

102 Samples and clinical data were received at the NRCM for routine typing and epidemiological  
103 surveillance that are institutional missions of the NRCM. Clinical information format was  
104 provided by the NRCM. Procedure of collecting samples and informations was submitted and  
105 approved by the CNIL N°1475242/2011 (*Commission Nationale de l'Informatique et des*  
106 *Libertés*). The patients were informed on the secondary use of samples/data and gave their  
107 consent for this use.

108

### 109 **Isolates and database**

110 This is a retrospective study using the database of the French National Reference Centre for  
111 Meningococci (NRCM) at the Institut Pasteur, Paris, France between 1991 and 2016. Isolates  
112 and samples corresponded to biological confirmed cases of IMD that were defined as a  
113 positive culture for *N. meningitidis* and/or positive testing PCR (used since 1998) in sterile  
114 sites. IMD cases were screened using the following key words for the clinical presentations:  
115 “abdominal pain” or “diarrhea” or “vomiting” or “peritonitis” or “appendicitis” or  
116 “appendicular syndrome” or “gastro-enteritis”. Cases were also screened for the site of  
117 sampling “peritoneal fluid”.

118

### 119 **Inclusion and exclusion criteria**

120 The cases included in the present study showed the following inclusion criteria: confirmed  
121 diagnosis of IMD and at least one abdominal symptom within the 24h before IMD diagnosis  
122 (i) abdominal pain only, (ii) gastro-enteritis with diarrhea and vomiting, (iii) or diarrhea only.  
123 Cases with associated co-morbidities that may explain abdominal symptoms were excluded.

124 Vomiting in the context of the meningeal syndrome without any other abdominal symptoms  
125 were not retained.

126

### 127 **Clinical and biological data**

128 Available epidemiological data (age, sex), clinical and biological data (C-reactive protein  
129 (CRP) in blood), were collected from NRCM database or from medical reports of  
130 hospitalization obtained after contact (phone, mail) of the different hospitals.

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### 132 **Bacterial whole genome sequencing**

133 PCR-confirmed cases were typed by MLST analysis and all cultured isolates were typed by  
134 WGS. Typing data were expressed as a genetic formula (g :P1.PorA-VR1, PorA-  
135 VR2:FetA :cc) that define the group (g), the two variable regions (VR1 and VR2) of the outer  
136 membrane protein PorA, and of the VR of the protein FetA, as well as the clonal complex  
137 (cc).

138 In this manuscript, group "g" will be used to refer to both serogroup and genogroup to  
139 characterise cultured-confirmed and PCR-confirmed cases respectively. WGS was performed  
140 by Illumina HiSeq 2000 sequencer (Illumina, San Diego, CA, USA) and assembled as  
141 previously described [13]. Sequences are available through the PubMLST database which  
142 runs on the Bacterial Isolate Genome Sequence Database (BIGSdb) platform [14]. WGS data  
143 were analyzed using a "gene-by-gene" approach available through the PubMLST Genome  
144 Comparator tool using *N. meningitidis* core genome v1.0 that includes 1605 core loci [14].  
145 SplitsTree4 (version 4.13.1) was used to visualize the resulting distance matrices as  
146 Neighbour-net networks [15]. Further genomic analysis were performed for the period 2010-  
147 2016 to compare the NmW isolates of cc11 with abdominal presentations to all the NmW  
148 isolates belonging to the cc11 in France [16]. The IDs of all culture isolates are given in the

149 supplementary Table 1 to allow retrieving of WGS sequence in FASTA formats. Loci with  
150 alleles specific to isolates of serogroup W belonging related to the South American UK strains  
151 were characterized according to the KEGG Orthology (KO) groupings of the KEGG database  
152 ([www.kegg.jp](http://www.kegg.jp)).

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154 **Statistical analysis:**

155 Data were analysed using the chi-square test, Student's t-test and analysis of variance  
156 (ANOVA), with  $p < 0.05$  considered to be statistically significant.

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174 **Results**

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176 **Clinical data of IMD patients with abdominal presentations**

177 One hundred fourteen patients with abdominal presentation of IMD were initially  
178 selected between 1991 and 2016, according to criteria of inclusion. Among these patients, 9  
179 were excluded for the following reasons: (i) 3 patients had abdominal pain with constipation,  
180 (ii) 2 patients had diarrhea 24h after the diagnosis of IMD and after starting antibiotic  
181 treatment (iii) 1 patient had salpingitis with no link to the IMD, (iv) 2 patients had cirrhosis  
182 and (v) 1 patient had an abdominal trauma. The final study population consisted of 105  
183 patients with abdominal presentations of IMD. These cases corresponded to 92 culture-  
184 confirmed cases and 13 PCR-confirmed cases (Fig.1). The clinical data and characteristics of  
185 the patients were depicted in Table 1. The male/female ratio was 0.81 (47 males and 58  
186 females). The median age for all the 105 cases was 19 years (Interquartile range (Q1-Q3: 6.5-  
187 50): 14 years for group B “gB” meningococci cases (Q1-Q3: 2-51), 18 years for gC cases  
188 (Q1-Q3: 8-35), 26 years for gW cases (Q1-Q3: 16.5-54.5) and 26 years for gY (Q1-Q3: 18-  
189 71.5). One case was due to gX (female of 78 years old). After the admission to the hospital,  
190 cases were confirmed as IMD from CSF (n=25; 23%), from blood (n=67; 64%), from both  
191 CSF and blood (n=9; 9%) and from peritoneal fluid (n=4; 4%).

192 The most frequent abdominal symptom was the abdominal pain only (n=67, 64%). One  
193 quarter of the cohort had gastro-enteritis (n=26, 25%) and diarrhea only represented 11% of  
194 the cohort (n=12). CRP levels was available for 58 cases with a mean value of 198 mg/L (the  
195 95% confidence interval was (161-235)). In 20% of the cohort (n=20), the abdominal  
196 presentations at the admission led to an abdominal surgery on the basis of fever and the  
197 location of the pain in the right iliac fossa. The case fatality rate (among the 79 cases with  
198 known evolution) was 24% in these IMD cases with abdominal presentations and was

199 significantly higher than that of all IMD (10.4%;  $p=0.007$ ) and remain significant ( $p=0.01$ )  
200 even if all patient with missing evolution data survived. There was no significant difference in  
201 the fatality rate between cases with or without abdominal surgery.

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### 203 **Bacteriological characteristics of IMD with abdominal presentations**

204 Cases with abdominal presentation ( $n=105$ ) were compared to all cases of IMD ( $n=11979$ )  
205 addressed to CNRM in Paris during the period of the study. Two periods of increase of  
206 diagnosis of cases with abdominal presentation were observed (Fig. 2). The first was in the  
207 early 2000's that paralleled an increase in total cases and a predominance of serogroup C (Fig.  
208 2). The second period showed a sharp increase that was observed since 2014.

209 The most frequent group among IMD cases with abdominal presentation was group C  
210 followed by group B (Table 2). Group W cases ranked third, followed by group Y. However,  
211 serogroup W cases increased rapidly since 2014, concomitantly with the sharp increase of  
212 IMD cases with abdominal presentation since 2014 (Fig. 2).

213 There was a significant lower proportion of group B among cases with abdominal  
214 presentations compared to all cases of IMD. At the opposite, there were significant higher  
215 proportions of groups C and W among cases with abdominal presentations compared to all  
216 cases of IMD (Fig. 3). Clonal complexes data were available for 96 cases of all 105 cases  
217 with abdominal presentations (91%). The cc11 was responsible for most of the cases with 43  
218 cases (45%) with 33 cases due to NmC-cc11 and 10 cases due to NmW-cc11. We also  
219 compared the distribution of clonal complexes for IMD cases with abdominal presentations to  
220 that for all IMD. This analysis focused on the period 2010-2016 for which the MLST data  
221 were available at the CNRM for at least 89% of all IMD cases (MLST data were available for  
222 2891 cases of 3245 IMD total cases with percentage of completeness ranging for the period  
223 2010-2016 between 87% to 94%). There were 27 cases (5 of group B, 7 group of C, 10 group

224 W, 4 of group Y and 1 of group X) of IMD with abdominal presentations and with MLST  
225 data. Similar to the whole period of the study, the distribution of cases of groups B and W for  
226 the period 2010-2016 differed significantly between all IMD cases and cases with abdominal  
227 presentations: the proportions of group B cases were respectively 62% versus 29% and that of  
228 group W were respectively 6% versus 29% with  $p$  values of 0.01 and  $<0.00001$  respectively.  
229 Moreover, the proportion of cc11 cases ( $n=17$ ; 63%) was significantly higher than that for all  
230 IMD ( $n=709$ ; 25% respectively,  $p<0.0001$ ) (Fig. 4). Ten of these cc11 isolates belonged to  
231 group W and 7 isolates to group C.

232

### 233 **Whole genome sequencing analysis of isolates from IMD with abdominal presentations**

234 A core genome MLST tree was performed on all the 92 cultured isolates of cases with  
235 abdominal presentation with a structure similar to that usually observed with invasive isolates  
236 from IMD (Fig. 5). The 92 isolates were distributed mainly in the hyperinvasive clonal  
237 complexes, in particular, the cc11 that included mainly isolates of groups C and W. While  
238 group C isolates were in several lineages of cc11, group W isolates were all within one  
239 lineage (Supplementary figure and Fig. 6). The recent rapid increase of cases with abdominal  
240 presentation due to serogroup W prompted us to explore the genomic relationships of these  
241 isolates with the circulating strains in Europe (the South American-UK strain and Anglo-  
242 French Hajj strain). We recently reported the resolution of all invasive group W isolates in  
243 France between 2010 and 2016 ( $n=132$  cases)[16]. We therefore analyzed the core genome  
244 MLST tree of these isolates according to the presence of abdominal presentations and  
245 identified on the tree the cases with these presentations (Fig.6). All isolates of the cases with  
246 abdominal presentation were exclusively located within the two sublineages of the South  
247 American-UK strain (the original UK strain” and the “UK 2013-strain). The cases with  
248 abdominal presentation represented 7.6% ( $n=10$ ) of all IMD W cases for this period ( $n=132$ )

249 but they represented 17% (n=10) of the cases due to isolates belonging South American-UK  
250 strain (n=59). No major difference was detected between isolates with abdominal presentation  
251 and other isolates derived from South American-UK strain. However, 119 loci were identical  
252 in all group W/cc11 isolates of the two sublineages of the South American-UK strain but  
253 differed from the isolates of group W/cc11 belonging to the Anglo-French Hajj strain  
254 (Supplementary Table 2). These genes were distributed all over the chromosome. The  
255 annotation of these specific alleles revealed characterized function for 57.1% of these loci  
256 while there was no characterized function for 42.9 %. The annotated functions were:  
257 metabolic functions (35.3%); genetic information processing (14.1%); environmental  
258 information processing (5%); cellular processes (1%) and antigenic genes (1.7%). The  
259 antigenic genes were the genes encoding factor H binding protein (fHbp) and Neisseria  
260 heparin binding antigen (NHBA) two proteins involved in the meningococcal survival in body  
261 fluids through modulating the interaction with components of the innate immune response.  
262 These two proteins are also included in the proteins-based vaccines targeting group B isolates.

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274 **Discussion**

275 We reported a large cohort of patients including 105 cases with initial abdominal presentation  
276 of IMD during the 24h prior to the diagnosis. The first report of acute abdominal syndromes  
277 of invasive meningococcal infection was published in 1917 [17]. Since then, few case-reports  
278 have been described [18]. We were able to find 105 cases in 27 years in France in our study  
279 (1% of all the 11979 IMD during this period). However, this presentation may be overlooked  
280 resulting in underestimation of these forms. Abdominal symptoms like abdominal pain,  
281 diarrhea, vomiting are not specific and may evoke viral infections as major differential  
282 diagnosis. The abdominal pain alone was the most frequent (64%) early presentation among  
283 these abdominal forms. Moreover, the localization of abdominal pain during IMD is  
284 frequently around the right iliac fossa that may be misleading, as it would invoke “acute  
285 abdomen” leading to urgent, but unwarranted, surgical intervention for an acute appendicitis  
286 [19-23]. This may explain the high rate of morbidity in our study with 20% of unjustified  
287 abdominal surgery. Abdominal pain may be overlooked in young children. This is an  
288 important limitation to our retrospective study that may impact on the variable that were  
289 analyzed. However, this point further underline the underreporting of abdominal presentation  
290 of IMD. The missing data on survival for 26 cases is another limitation to this retrospective  
291 study. In a review of 19 cases [18] of acute abdominal pain as initial presentation of IMD,  
292 42% of surgical procedures were reported following suspicion of acute abdomen. The high  
293 case fatality rate of 24% in our study is also worrying particularly when comparing to all  
294 cases of IMD in France which rate is 10.4% [24].

295 The recent increase of the cases with abdominal presentation since 2014 seems to be driven  
296 by the increase of IMD cases due to cc11 isolates of groups C and W. While group C isolates  
297 belonged to several lineages of cc11, group W isolates with abdominal presentation belonged  
298 exclusively to the lineage of the South American UK strain (Fig. 4 and Fig. 5). These

299 observations are in line with those obtained in the UK and in Chile [11, 12] suggesting that  
300 these isolates are significantly associated with abdominal presentations of IMD.

301 Although hyperinvasive NmW isolates of cc11 are related, several genetic changes seem to  
302 have occurred in the isolates belonging to the sublineages of the South-American-UK strain  
303 compared to the isolates belonging to the Anglo-French-Hajj strain. These events may have  
304 increased transmission leading to the recent expansion of the former isolates. These genetic  
305 differences concerned mainly genes encoding diverse metabolic classes of function  
306 (metabolism of carbohydrate, fatty acids amino-acids and nucleic acids). This observation is  
307 in agreement with the hypothesis linking the emergence of hyperinvasive pandemic lineages  
308 of meningococci group A in Sub-Saharan Africa to shifts in genes encoding metabolic  
309 functions [25]. Linking virulence and meningococcal carbohydrate metabolism has been also  
310 suggested [26, 27]. Changes in genes encoding metabolic functions may also impact genes  
311 involved in the biosynthesis of virulence factors in the bacterial wall such as the  
312 lipooligosaccharide and peptidoglycan that are potent inducers of inflammatory responses in  
313 meningococci [28]. Few other changes occurred in genes encoding proteins involved in  
314 virulence (such as fHbp and NHBA) that may impact on bacterial survival. These genetic  
315 changes may therefore also increase within-host fitness of the isolates and lead to increase  
316 virulence and the induction of strong inflammatory response. Although the pathophysiology  
317 of abdominal pain in IMD remains obscure, the induction of the inflammatory response may  
318 be involved. Several hypotheses are proposed such as mesenteric hypoperfusion or septic  
319 epiploic micro infarctions during the hematogeneous spread or immune complex deposition  
320 [18, 29]. Inflammation and detectable meningococci were recently reported in a duodenal  
321 biopsy during a case of meningococemia with abdominal pain due to an isolate of group W  
322 [30].

323 In conclusion, abdominal presentation of IMD seems to increase and to be associated with the  
324 worldwide expanding NmW/cc11 isolates of the South American-UK strain [5, 6]. Clinicians  
325 should be aware of this atypical presentation in the differential diagnosis of fever with  
326 abdominal pain to avoid delay of management of IMD.

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348 **Author's contributions**

349 All authors participated in the design, analysis and interpretation of the study. MKT, TG and  
350 AED were involved in all phases of the study. MKT, TG and MG performed data extraction,  
351 analyzed patient data, statistical analysis, and made the bibliographic search. AED, EH, AT,  
352 MD performed the bacteriological typing. MKT and TG wrote the manuscript and all authors  
353 assisted with manuscript writing and editing.

354

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365 **Declaration of interests**

366 All authors declare no conflicts of interest.

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## Legends of figures

### **Figure 1. Flow chart of the study**

**Figure 2. Distribution of IMD cases during the period 1991-2016.** Annual distribution of numbers of all IMD cases (left side axis) and numbers of IMD cases with abdominal presentation (right axis) are shown. All the cases (all serogroups) are presented as well as cases due to the most frequent groups (B, C and W) as indicated above each graph.

**Figure 3. Percentage of groups B, C, W, Y and X among all IMD cases or cases with abdominal presentations.** All the cases for each group are shown with the 95% confidence intervals for the whole study period 1991-2016. Asterisk indicate statistical significance ( $*p<0.01$ ,  $**p<0.001$  and  $***p<0.0001$ ).

**Figure 4. Distribution of cases of IMD according to groups (A) or clonal complexes (B) during the period 2010-2016.** The data are presented as percentage for all IMD cases (1) or cases with abdominal presentation (2). The corresponding years are indicated under each presentation.

**Figure 5. Neighbour-net phylogenetic network of all the cultured isolates from IMD cases with abdominal presentations.** The tree was performed on the basis of cgMLST. The groups are represented in different colours as indicated and the major clonal complexes (cc) are indicated in dashed lines.

**Figure 6. Neighbor-net phylogenetic network of all IMD cases due to NmWcc11 cases in France for the period 2010-2016.** NmW/cc11 cases with abdominal presentations are indicated in black circles. Dashed lines indicate the isolates that belonged to the Anglo-French-Hajj strain, the “original UK strain” and the “UK 2013-strain”.

**Table 1 Clinical characteristic of patients with abdominal presentations**

Sex ratio (male/female)	0.81
Median age (range)	19 years (0.2-91)
Abdominal symptoms n, (%)	
Abdominal pain only, n (%)	67 (64)
Gastro-enteritis, n (%)	26 (25)
Diarrhea only n (%)	12 (11)
Abdominal surgery, n (%) (n=100)*	20 (20)
Other clinical symptoms	
Purpura n (%) (n=84)*	30 (36)
Meningeal irritation n (%) (n=81)*	41 (51)
Death, n (%) (n=79)*	19 (24)
Site of sampling	
Blood n (%)	67 (64)
CSF n (%)	25 (23)
Both n(%)	9 (9)
Peritoneal liquid n (%)	4 (4)

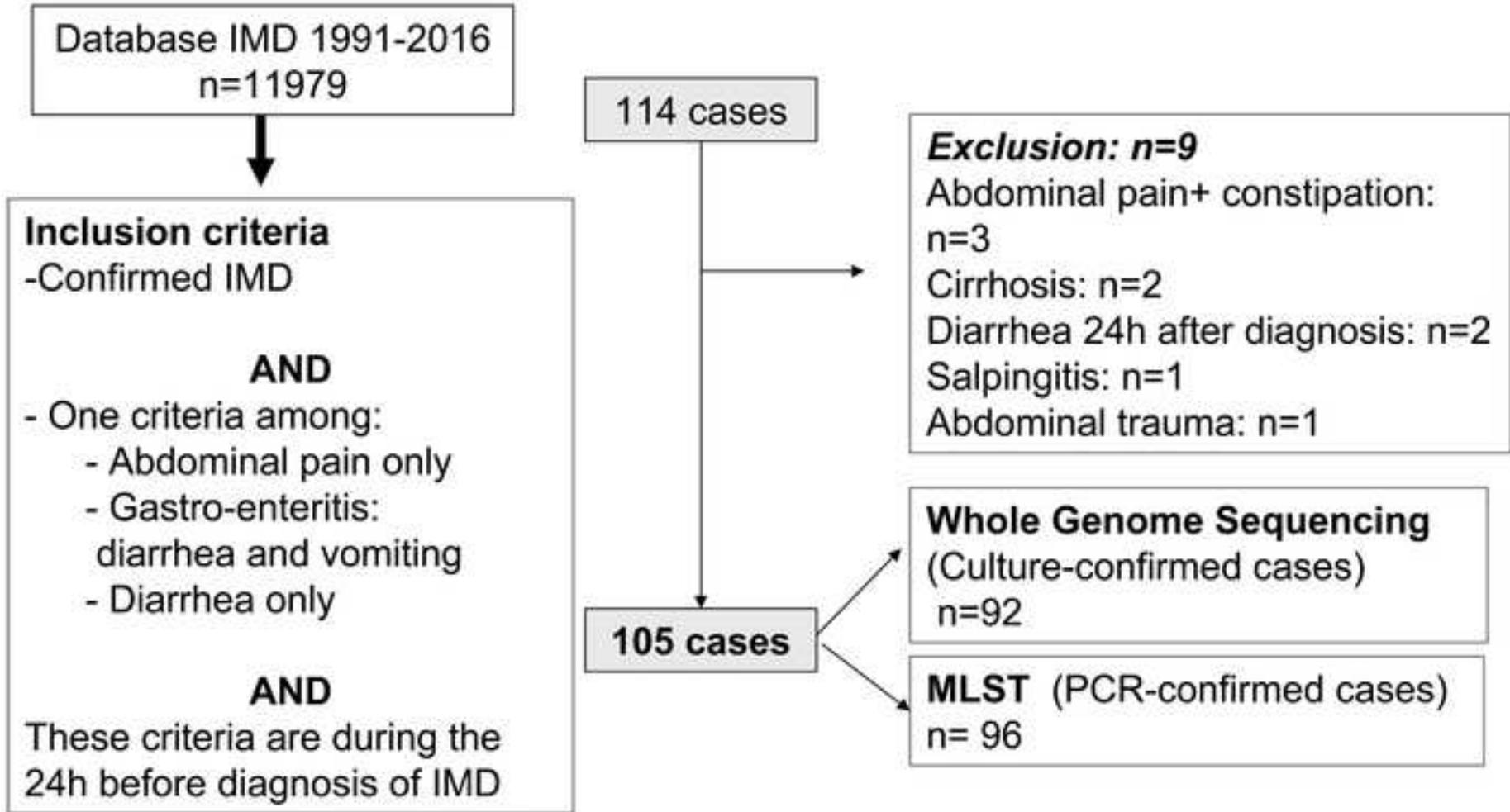
\*Total number of cases for which the corresponding data were available

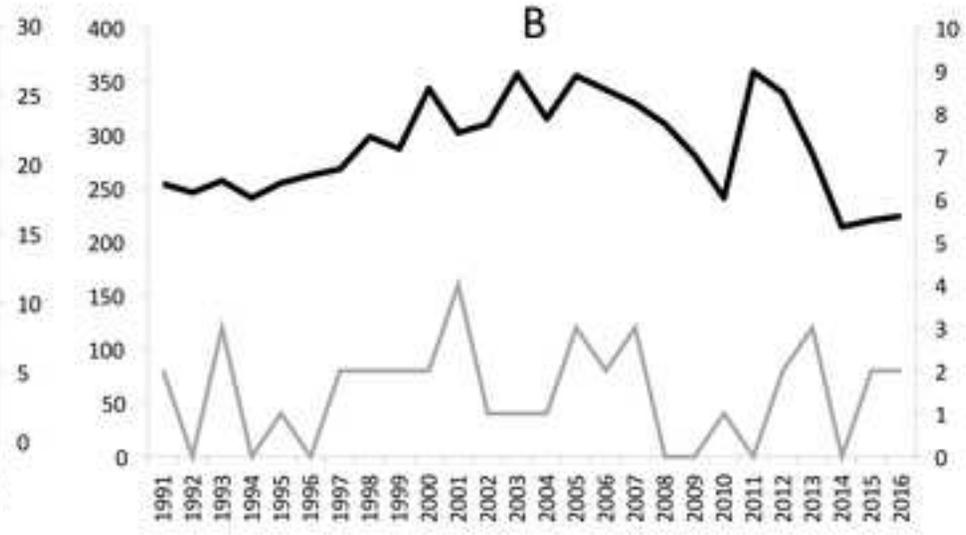
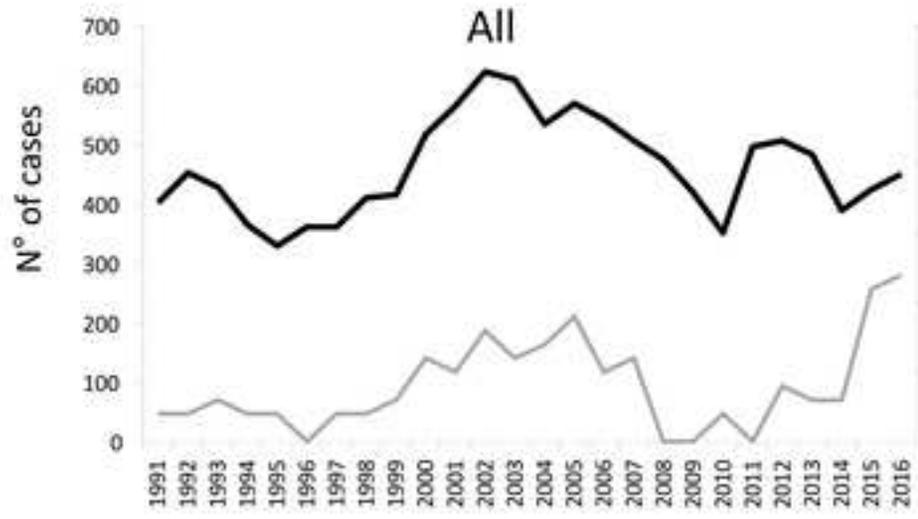
**Table 2 Bacterial characteristics of isolates from patients with abdominal presentations**

Bacterial Markers	Values
Group n (%)	
B	35 (33)
C	44 (42)
Y	8 (8)
W	17 (16)
X	1 (1)
Clonal Complexes n (%)**	
cc11	43 (45)
cc32	10 (10)
cc41/44	9 (9)
cc269	2(2)
Other cc and non-assigned	32 (34)

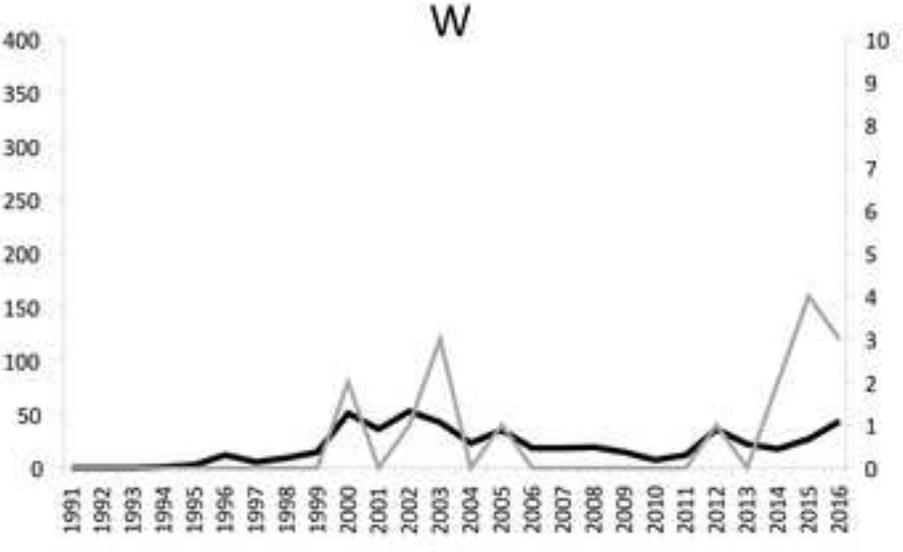
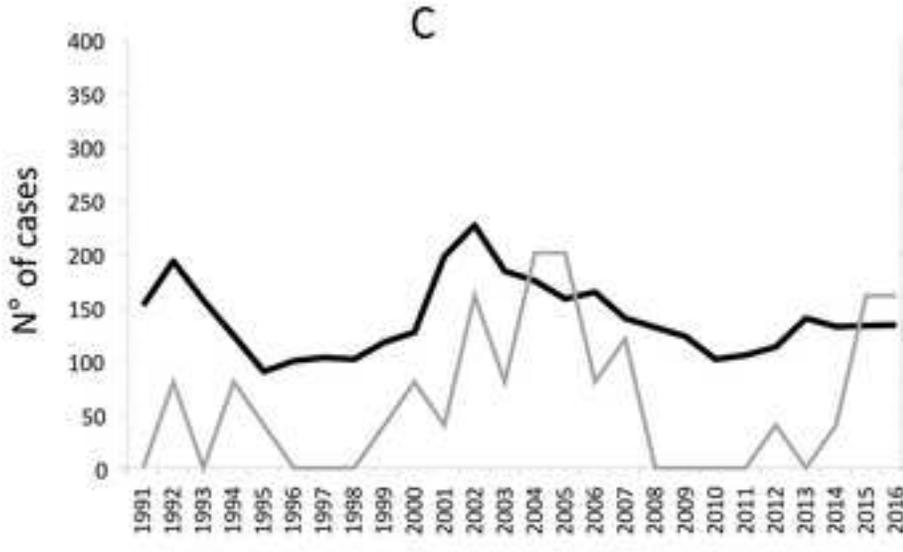
\*Total number of cases for which the corresponding data were available

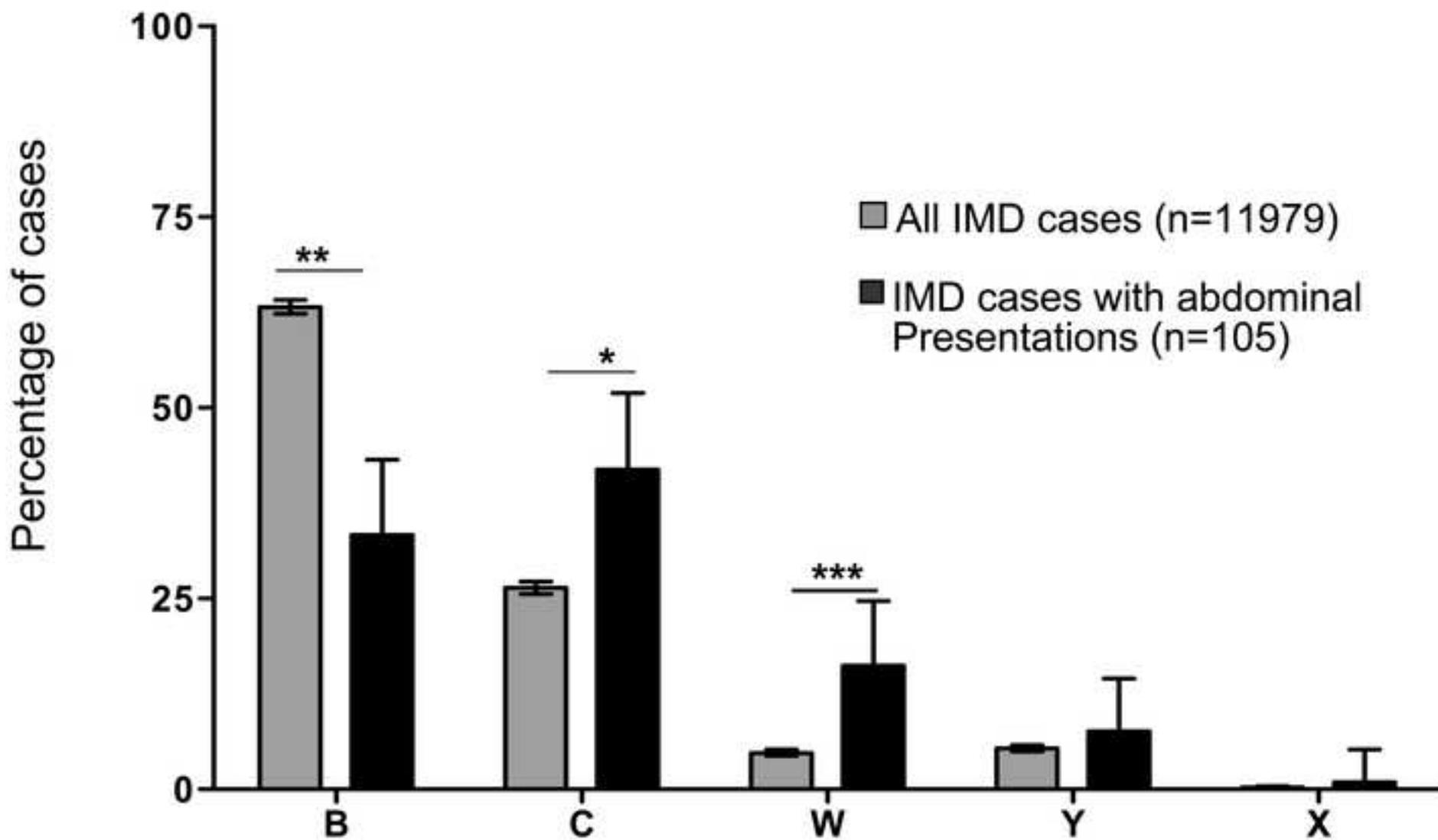
\*\*Data for 96 cases with available cc

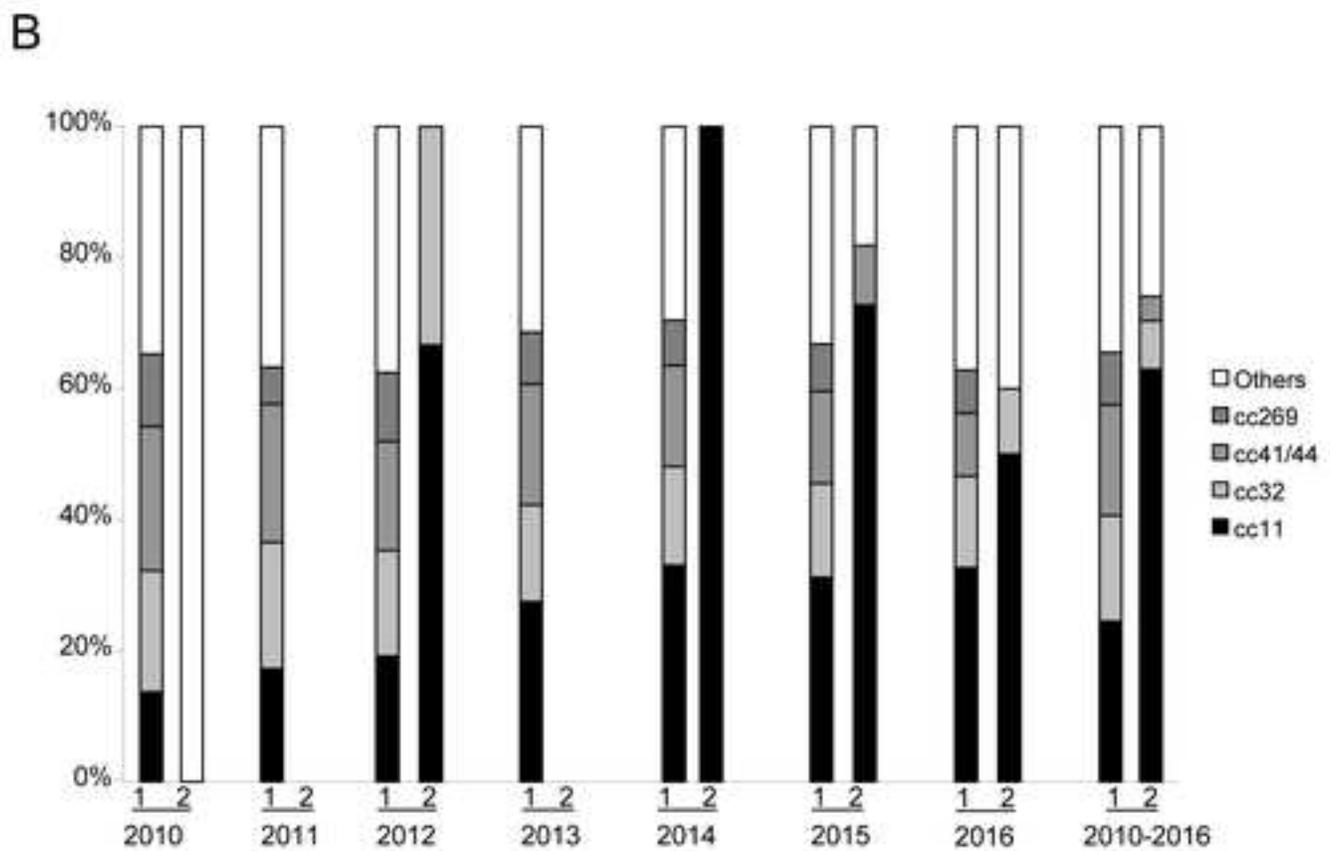
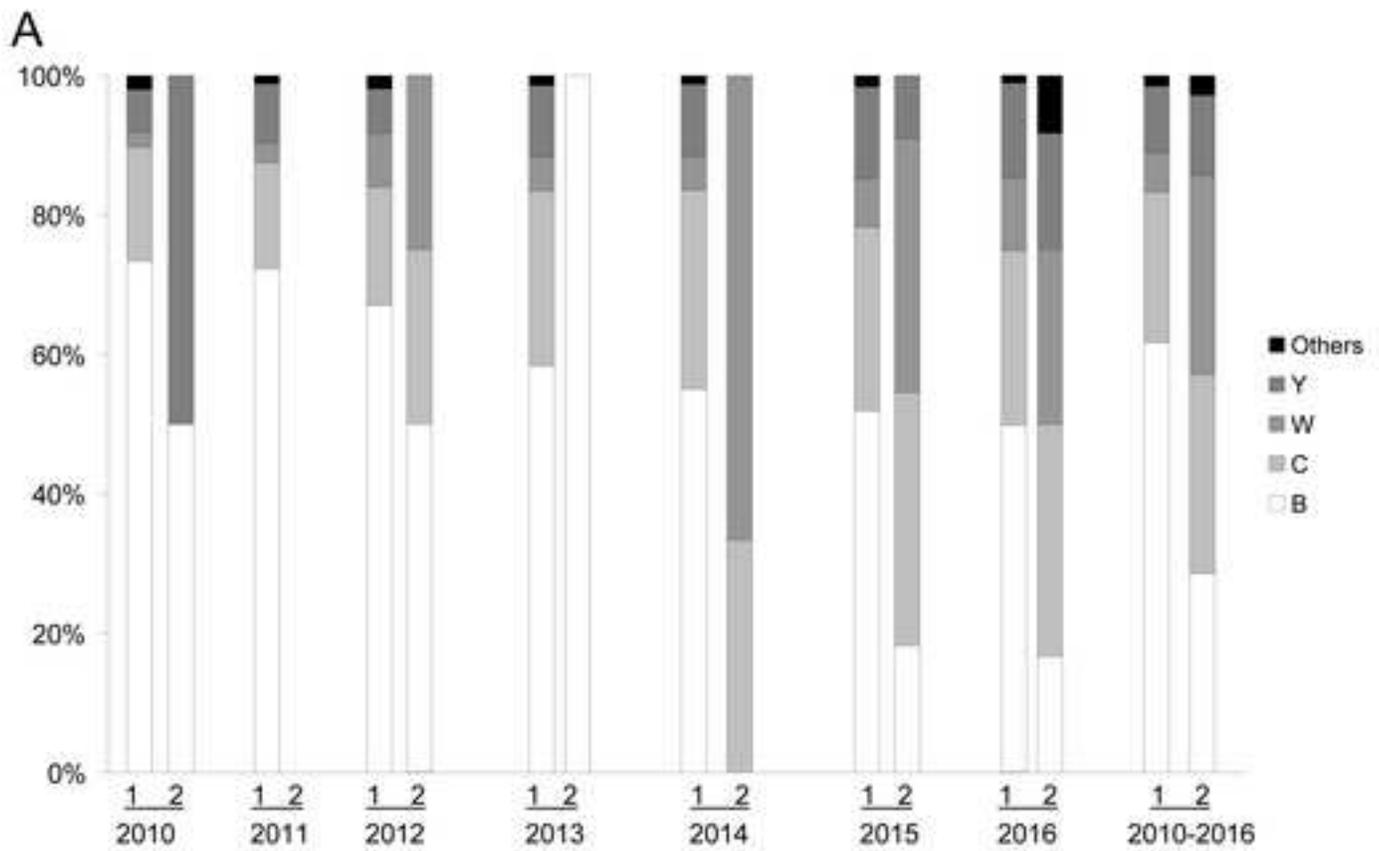


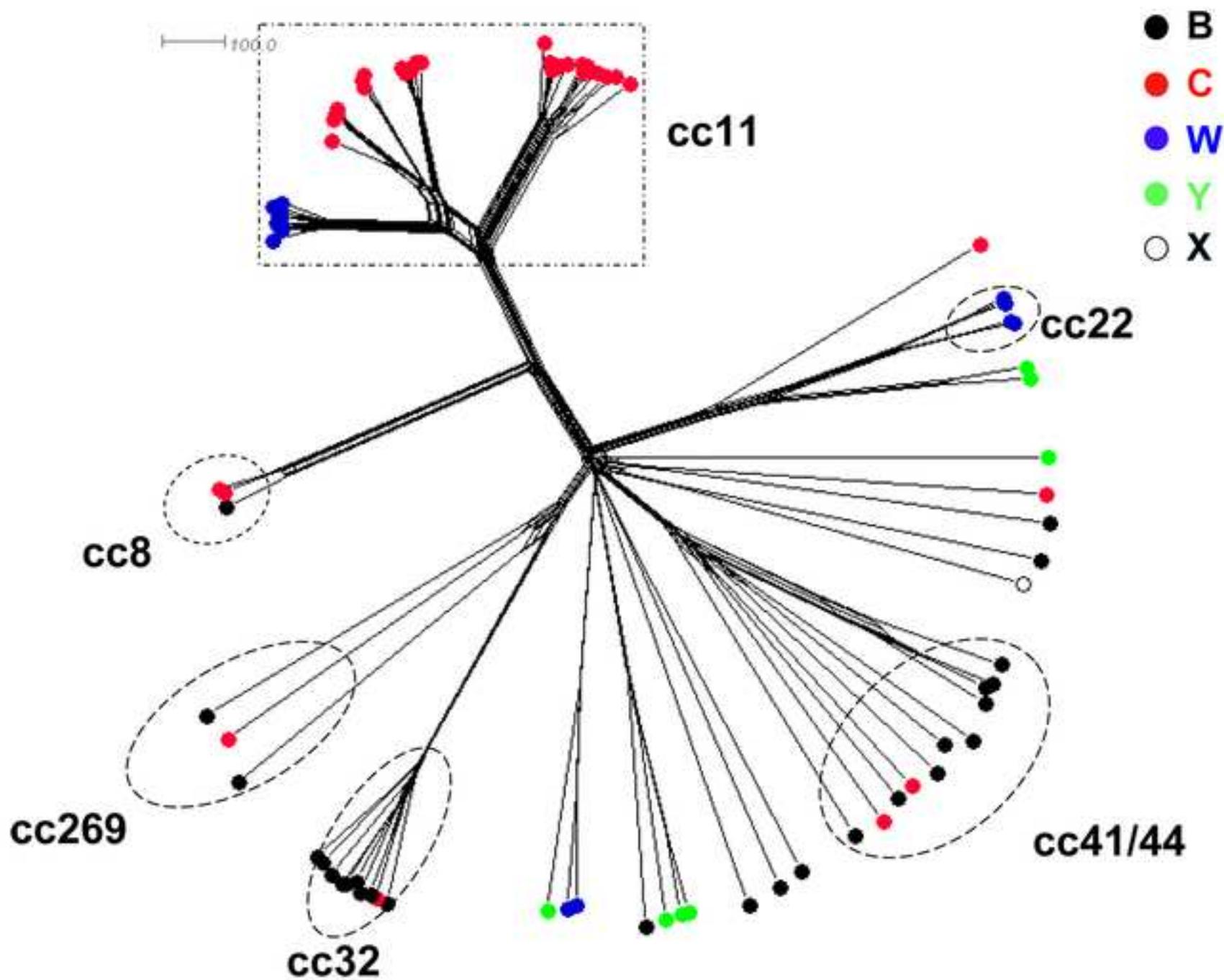


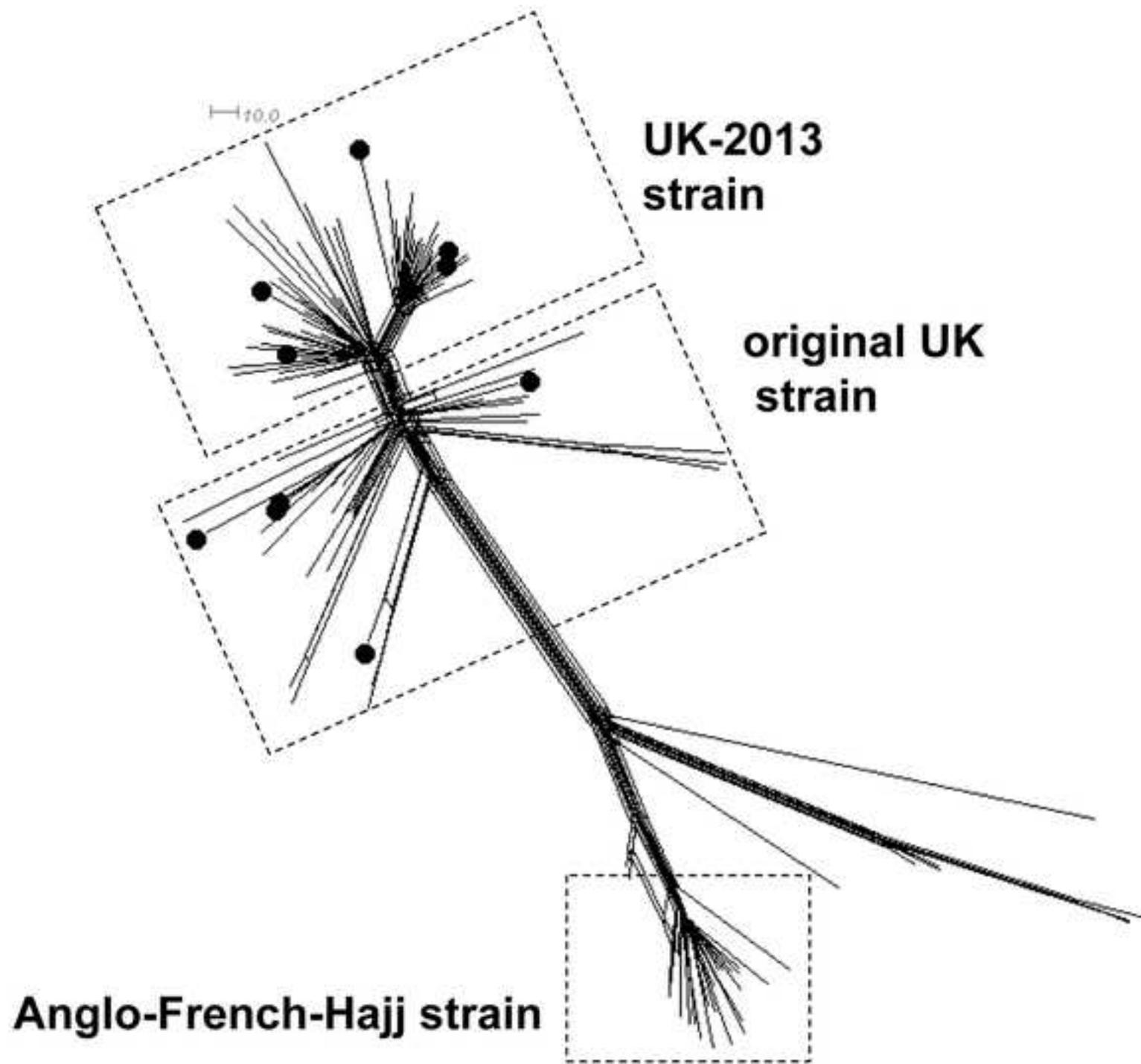
— All IMD cases  
— IMD cases with abdominal presentation











Supplementary Table 1

id	isolate	year	serogroup	PorA_VR1	PorA_VR2	FetA_VR	ST (MLST)	clonal_complex (MLST)
40273	LNP28343abd	2015	Y	5-1	10-8	F3-6	1627	ST-167 complex
40279	LNP28349abd	2015	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
40387	LNP28359abd	2015	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
41586	LNP28420abd	2016	C	5	2	F3-3	11	ST-11 complex/ET-37 complex
41857	LNP28585abd	2016	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
42399	LNP28519abd	2016	B	5	2	F2-9	33	ST-32 complex/ET-5 complex
42440	LNP28527abd	2016	B	17	16-3	F5-5	3989	NA
44056	LNP28630abd	2016	Y	18-1	3	F3-4	3015	NA
46093	LNP28706abd	2016	X	5-1	2-2	F5-1	10948	NA
46100	LNP28713abd	2016	Y	18-1	3	F3-4	5436	NA
46745	LNP28054abd	2015	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
46748	LNP28099abd	2015	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
49253	LNP28772abd	2016	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
49303	LNP28792abd	2016	C	5	2	F3-3	11	ST-11 complex/ET-37 complex
50819	LNP26753abd	2012	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
50850	LNP27754abd	2014	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
50856	LNP27907abd	2014	W	5	2	F1-1	1237	ST-11 complex/ET-37 complex
51010	LNP28840abd	2016	W	5	2	F1-1	11	ST-11 complex/ET-37 complex
54270	LNP10941abd	1992	C	22-1	14	F1-5		ST-269 complex
54563	LNP10049abd	1991	B	18-1	30-2	F3-6	8567	NA
54564	LNP10436abd	1991	C	12-1	13-1	F3-9		NA
54565	LNP11060abd	1992	C	5-1	10-4	F3-6	11	ST-11 complex/ET-37 complex
54566	LNP11548abd	1993	C	5	2	F3-6	11	ST-11 complex/ET-37 complex
54567	LNP11972abd	1993	C	21	16	F3-6	11	ST-11 complex/ET-37 complex
54568	LNP12043abd	1993	C	5	2	F1-1	11	ST-11 complex/ET-37 complex
54569	LNP12355abd	1994	C	18-3	1	F5-3	206	ST-41/44 complex/Lineage 3
54570	LNP13122abd	1994	C	5	2	F3-6	11	ST-11 complex/ET-37 complex
54571	LNP13408abd	1995	C		2-2	F5-75	11	ST-11 complex/ET-37 complex
54572	LNP13755abd	1995	B	7	9	F5-1	33	ST-32 complex/ET-5 complex
54573	LNP15138abd	1997	B	7-2	13-9	F4-17	23	ST-23 complex/Cluster A3

54574	LNP15363abd	1997	B	22	26	F5-5		NA
54575	LNP16393abd	1998	B	7-2	4	F1-5	41	ST-41/44 complex/Lineage 3
54576	LNP16397abd	1998	B	7	16-26	F3-3	32	ST-32 complex/ET-5 complex
54577	LNP16739abd	1999	B	5-2	10	F4-1	291	ST-41/44 complex/Lineage 3
54578	LNP17159abd	1999	B	7-2	4	F1-5	42	ST-41/44 complex/Lineage 3
54579	LNP17561abd	2000	B	22		F1-15	213	ST-213 complex
54580	LNP17566abd	2000	W		1	F4-1	22	ST-22 complex
54581	LNP17987abd	2000	C	5	2-1	F5-5	11	ST-11 complex/ET-37 complex
54582	LNP17993abd	2000	W		1	F4-1	22	ST-22 complex
54583	LNP18254abd	2000	B	5-2	10-2	F1-1		ST-254 complex
54584	LNP18292abd	2000	C	5	2	F5-8	8	ST-8 complex/Cluster A4
54585	LNP18775abd	2001	B	5-1	10-4	F1-5	1403	ST-41/44 complex/Lineage 3
54586	LNP18914abd	2001	B	7	16-26	F3-3	6562	ST-32 complex/ET-5 complex
54587	LNP18915abd	2001	B	22	14	F5-1	34	ST-32 complex/ET-5 complex
54588	LNP18948abd	2001	B	22-1	14	F3-6	35	ST-35 complex
54589	LNP19006abd	2001	C	18-7	9	F1-7	571	ST-41/44 complex/Lineage 3
54590	LNP19020abd	2001	C	5	2	F3-6	11	ST-11 complex/ET-37 complex
54591	LNP19425abd	2002	B	12-1	13-1	F5-12	4520	ST-364 complex
54592	LNP19477abd	2002	C	18-1	30-1	F3-7	11	ST-11 complex/ET-37 complex
54593	LNP19808abd	2002	Y	5-2	10-2	F4-1		ST-23 complex/Cluster A3
54594	LNP19811abd	2002	W	5-1	10-4	F1-18	2495	ST-174 complex
54595	LNP19969abd	2002	C	7-1	1	F1-120	1306	ST-865 complex
54596	LNP20098abd	2002	Y	21	16	F3-7	1466	ST-174 complex
54597	LNP20214abd	2002	C	5	2-1	F5-5	11	ST-11 complex/ET-37 complex
54598	LNP20244abd	2002	C	5-1	10-8	F3-6	11	ST-11 complex/ET-37 complex
54599	LNP20320abd	2003	C	5	2-1	F5-5	11	ST-11 complex/ET-37 complex
54600	LNP20810abd	2003	C	5-1	10-8	F3-6	11	ST-11 complex/ET-37 complex
54601	LNP20813abd	2003	W	18-1	23	F4-1		ST-22 complex
54602	LNP20830abd	2003	W	5-1	10-52	F1-18	174	ST-174 complex
54603	LNP21088abd	2003	B	22	14-6	F1-7	146	ST-41/44 complex/Lineage 3
54604	LNP21202abd	2003	W	18-1	3	F4-1	184	ST-22 complex
54605	LNP21299abd	2004	C	5-1	10-8	F5-17	11	ST-11 complex/ET-37 complex
54606	LNP21447abd	2004	C	5	2	F5-9	11	ST-11 complex/ET-37 complex
54607	LNP21763abd	2004	Y	5-2	10-2	F2-13	23	ST-23 complex/Cluster A3
54608	LNP21819abd	2004	B	22	13-13	F1-5	8174	NA

54609	LNP21887abd	2004	C	5	2	F5-9	11	ST-11 complex/ET-37 complex
54610	LNP21936abd	2004	C	5	2	F5-9	11	ST-11 complex/ET-37 complex
54611	LNP22117abd	2004	C	5	2-1	F5-5	11	ST-11 complex/ET-37 complex
54612	LNP22143abd	2005	W	18-1	3	F4-1	22	ST-22 complex
54613	LNP22294abd	2005	B	7	16	F3-3	32	ST-32 complex/ET-5 complex
54614	LNP22323abd	2005	B	5	2	F5-8	8	ST-8 complex/Cluster A4
54615	LNP22516abd	2005	C	5	2-1	F5-5	11	ST-11 complex/ET-37 complex
54616	LNP22638abd	2005	C	5-1	10-8	F3-6	11	ST-11 complex/ET-37 complex
54617	LNP22840abd	2005	C	5	2	F5-5	8	ST-8 complex/Cluster A4
54618	LNP22912abd	2005	C	5	2	F3-3	11	ST-11 complex/ET-37 complex
54619	LNP23213abd	2006	C	7-1	1	F3-6	11	ST-11 complex/ET-37 complex
54620	LNP23290abd	2006	B	19-1	15-11	F5-1	269	ST-269 complex
54621	LNP23363abd	2006	C	7-1	1	F3-6	11	ST-11 complex/ET-37 complex
54622	LNP23532abd	2006	Y	5-1	10-1	F4-1	23	ST-23 complex/Cluster A3
54623	LNP23749abd	2006	B	7-2	13-2	F1-5	40	ST-41/44 complex/Lineage 3
54624	LNP24131abd	2007	B	7	16	F3-3	32	ST-32 complex/ET-5 complex
54625	LNP24174abd	2007	C	5-1	10-1	F5-5	11	ST-11 complex/ET-37 complex
54626	LNP24231abd	2007	C	7-2	16-29	F3-3	9074	ST-32 complex/ET-5 complex
54627	LNP24274abd	2007	C	5	2-1	F5-5	11	ST-11 complex/ET-37 complex
54628	LNP24347abd	2007	B	19	15	F5-1	2501	ST-32 complex/ET-5 complex
54629	LNP26521abd	2012	B	19	15	F5-91	33	ST-32 complex/ET-5 complex
54630	LNP26626abd	2012	C	7-4	1	F3-6	11	ST-11 complex/ET-37 complex
54631	LNP28018abd	2015	C	5	2	F3-3	11	ST-11 complex/ET-37 complex
54632	LNP28033abd	2015	C	5	2	F3-3	11	ST-11 complex/ET-37 complex
54633	LNP28072abd	2015	C	5	2	F3-3	11	ST-11 complex/ET-37 complex
54634	LNP28134abd	2015	C	5	2	F3-3	11	ST-11 complex/ET-37 complex
54635	LNP28229abd	2015	B	7-1	14	F1-96	303	ST-41/44 complex/Lineage 3

NA= Not assigned

Supplementary Table 2

LOCI	DESCRIPTION of the products	correspondance in NMB and NMC	Classes	Othets
NEIS0040	DnaK suppressor protein	NMB0056	RNA metabolism	
NEIS0118	transcription antitermination protein nusG	NMB0126	Genetic information processing	
NEIS0164	valyl-tRNA synthetase	NMB0174	Genetic Information Processing; Translation	tRNA metabolism,
NEIS0173	outer membrane protein OMP85	NMB0182; NMC0173	No hints in the KEGG database (www.kegg.jp)	
NEIS0203	L-serine dehydratase; NMB211, NMC0203, NGO1773	NMB211	Metabolism; Biosynthesis of other secondary metabolites	Biosynthesis of amino acids
NEIS0224	bifunctional glutamine-synthetase adenyltransferase/deadenyltransferase	NMB0224, NMC0224	Metabolism	
NEIS0242	NADH dehydrogenase I chain F	NMB0246, NMC0242	Metabolic pathways , Oxidative phosphorylation	
NEIS0306	hypothetical protein	NMB1917,NMC0306	No hints in the KEGG database (www.kegg.jp)	
NEIS0309	hypothetical protein	NMB1914, NMC0309	No hints in the KEGG database (www.kegg.jp)	
NEIS0320	chromosomal replication initiation protein	NMB1903; NMC0320	Environmental Information Processing; Signal transduction	Two-component system chemotaxis
NEIS0326	leucyl-tRNA synthetase	NGO0006; NMB1897; NMC0326	Genetic Information Processing; Translation	tRNA metabolism,
NEIS0336	protein-L-isoaspartate O-methyltransferase	NMB1885; NMC0336	Metabolism; Lipid metabolism	Fatty acid metabolism
NEIS0339	hypothetical protein	NGO0022; NMB1881; NMC0339	No hints in the KEGG database (www.kegg.jp)	
NEIS0345	orotate phosphoribosyltransferase pyrE	NMB1874; NMC0345	Metabolic pathway Pyrimidine metabolism -	
NEIS0346	hypothetical protein	NGO0030; NMB1873; NMC0346	Genetic Information Processing; Replication and repair	
NEIS0347	putative acetyltransferase	NMB1872; NMC0347	No hints in the KEGG database (www.kegg.jp)	
NEIS0348	hypothetical protein	NGO0032; NMB1871; NMC0348	No hints in the KEGG database (www.kegg.jp)	
NEIS0349	Factor H binding protein lipoprotein	NMB1870	Antigenic gene	

NEIS0350	fructose-1,6-bisphosphate aldolase (EC 4.1.2.13)	NMB1869	Metabolic pathways, Carbon metabolism	
NEIS0351	putative integrase/recombinase	NMB1868; NMC0351	Metabolism; Carbohydrate metabolism	Carbon metabolism
NEIS0443	TpsA activation/secretion protein TpsB	NMB1780; NMC0443	No hints in the KEGG database (www.kegg.jp)	
NEIS0491	primosome assembly protein PriA	NMB0551; NMC0491	Genetic Information Processing; Replication and repair	Homologous recombination
NEIS0499	hypothetical protein	NMB0558; NMC0499	No hints in the KEGG database (www.kegg.jp)	
NEIS0516	glycine cleavage system aminomethyltransferase T	NMB0574; NMC0516	Metabolism; Carbohydrate metabolism	Carbon metabolism
NEIS0545	putative nucleotide-binding protein	NMB0602; NMC0545	No hints in the KEGG database (www.kegg.jp)	
NEIS0550	preprotein translocase subunit SecD	NGO0189; NMB0607; NMC0550	Genetic Information Processing; Folding, sorting and degradation, transport	Protein export
NEIS0580	argH argininosuccinate lyase	NMB0637, NMC0580	Metabolic pathways; Biosynthesis of amino acids	
NEIS0582	putative deoxyribonucleotide triphosphate pyrophosphatase	NMB0639; NMC0582	Metabolism; Nucleotide metabolism	Purine metabolism
NEIS0583	hypothetical protein	NGO0222; NMB0640; NMC0583	No hints in the KEGG database (www.kegg.jp)	
NEIS0584	inorganic pyrophosphatase	NMB0641; NMC0584	Metabolism; Energy metabolism; Oxidative phosphorylation	
NEIS0585	ntpA dATP pyrophosphohydrolase	NGO0224; NMB0642; NMC0585; NMV_1767	Metabolism; Metabolism of cofactors and vitamins	Folate biosynthesis
NEIS0611	hypothetical protein	NGO0232; NMB0662; NMC0611	No hints in the KEGG database (www.kegg.jp)	
NEIS0632	lipoprotein	NGO0252	No hints in the KEGG database (www.kegg.jp)	
NEIS0641	amidophosphoribosyltransferase	NGO0263; NMB0690; NMC0641	Metabolism; Nucleotide metabolism; Amino acid metabolism	
NEIS0654	ribosomal large subunit pseudouridine synthase D	NGO0278; NMB0704; NMC0654	No hints in the KEGG database (www.kegg.jp)	
NEIS0655	transmembrane transport protein	NMB0705; NMC0655	No hints in the KEGG database (www.kegg.jp)	
NEIS0659	hypothetical protein	NGO0284; NMB0709; NMC0659	No hints in the KEGG database (www.kegg.jp)	
NEIS0695	hypothetical protein	NGO0319; NMB0741;	No hints in the KEGG database	

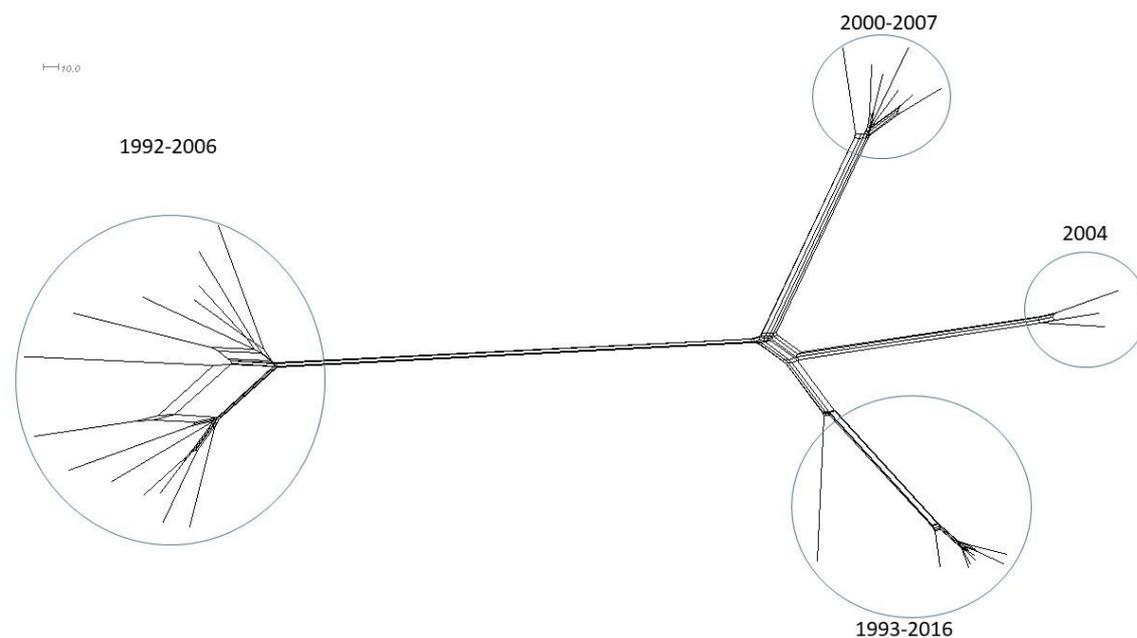
		NMC0695	(www.kegg.jp)	
NEIS0710	polynucleotide phosphorylase/polyadenylase	NGO0335; NMB0758; NMC0710	Metabolism; Nucleotide metabolism	
NEIS0718	signal peptidase I	NGO0343; NMB0765; NMC0718	Cellular Processes; Cellular community - prokaryotes+Genetic Information Processing; Folding, sorting and degradation	Quorum sensing; Protein export
NEIS0742	putative amino acid permease ATP-binding protein	NGO0374; NMB0789; NMC0742	Environmental Information Processing; Membrane transport	ABC Transporter
NEIS0794	histidyl-tRNA synthetase	NGO0426; NMB0854; NMC0794	Genetic Information Processing; Translation	tRNA metabolism,
NEIS0865	prophage-like protein	Vide	No hints in the KEGG database (www.kegg.jp)	
NEIS0944	putative outer-membrane receptor protein	NMB0964; NMC0944	No hints in the KEGG database (www.kegg.jp)	
NEIS0958	pyridine nucleotide transhydrogenase	NMB0978; NMC0958	Metabolism; Metabolism of cofactors and vitamins	Nicotinate and nicotinamide metabolism
NEIS0960	NAD(P) transhydrogenase subunit alpha	NMB0980; NMC0960	Metabolism; Metabolism of cofactors and vitamins	Nicotinate and nicotinamide metabolism
NEIS0961	phosphoserine phosphatase	NMB0981; NMC0961	Metabolism; Energy metabolism	
NEIS0966	phage-related protein	NMB0986	No hints in the KEGG database (www.kegg.jp)	
NEIS0984	D-lactate dehydrogenase	NMB0997; NMC0984	Metabolism; Carbohydrate metabolism	pyruvate
NEIS0995	hypothetical protein	NMB1003	No hints in the KEGG database (www.kegg.jp)	
NEIS1062	ABC transporter ATP-binding protein	Vide	Environmental Information Processing; Membrane transport	
NEIS1063	putative periplasmic protein	NGO0835; NMB1124; NMC1063	No hints in the KEGG database (www.kegg.jp)	
NEIS1065	hypothetical protein	NMB1125	No hints in the KEGG database (www.kegg.jp)	
NEIS1066	putative periplasmic protein	NGO0834; NMB1126; NMC1066	No hints in the KEGG database (www.kegg.jp)	
NEIS1067	short chain dehydrogenase	NGO0832; NMB1127; NMC1067	Metabolism	
NEIS1068	putative oxidoreductase	NGO0831; NMB1128;	Metabolism	

		NMC1068		
NEIS1070	hscA chaperone protein HscA	NMB1131	Genetic Information Processing	
NEIS1078	acetyl-CoA carboxylase carboxyltransferase subunit alpha	NGO0821; NMB1139; NMC1078	metabolism; Microbial metabolism in diverse environments	carbon; fatty acid; pyruvate; metabolism
NEIS1087	putative biotin synthase	NMB1146; NMC1087	Metabolism; Metabolism of cofactors and vitamins	
NEIS1090	dihydroxy-acid dehydratase	NMB1150;NMC1090	Metabolism; Microbial metabolism in diverse environments	
NEIS1117	hypothetical protein	Vide	No hints in the KEGG database (www.kegg.jp)	
NEIS1126	ABC transporter ATP-binding protein	NMB1226	Environmental Information Processing; Membrane transport	
NEIS1188	putative dnaJ-family protein	NMB1027; NMC1188	No hints in the KEGG database (www.kegg.jp)	
NEIS1219	hypothetical protein	NMB1284; NMC1219	No hints in the KEGG database (www.kegg.jp)	
NEIS1253	hypothetical protein	NMB1317A; NMC1253	No hints in the KEGG database (www.kegg.jp)	
NEIS1298	exodeoxyribonuclease VII large subunit	NMB1363; NMC1298	Genetic Information Processing; Replication and repair	
NEIS1365	transcription elongation factor GreA	NMB1430; NMC1365	Genetic information processing	
NEIS1370	putative integral membrane protein	NMB1435; NMC1370	No hints in the KEGG database (www.kegg.jp)	
NEIS1420	hypothetical protein	NMB1485; NMC1420	No hints in the KEGG database (www.kegg.jp)	
NEIS1436	arginyl-tRNA synthetase	NMB1506; NMC1436	Genetic Information Processing; Translation	tRNA metabolism,
NEIS1465	DNA primase	NMB1146; NMC1087	Metabolism; Metabolism of cofactors and vitamins	
NEIS1486	phosphoribosylglycinamide transformylase	NMB1566; NMC1486	No hints in the KEGG database (www.kegg.jp)	
NEIS1503	imidazoleglycerol-phosphate dehydratase	NMB1583; NMC1503	Metabolism; Amino acid metabolism	Biosynthesis of amino acids
NEIS1549	AniA nitrite reductase, major outer membrane copper-containing protein	NMC1549	Metabolism; Energy metabolism	Nitrogen metabolism
NEIS1554	SerC phosphoserine aminotransferase	NMB1640; NMC1554	Metabolism; Amino acid metabolism	Biosynthesis of amino acids
NEIS1564	putative disulphide bond formation	NMB1649; NMC1564	No hints in the KEGG database	

	protein		(www.kegg.jp)	
NEIS1590	putative lipoprotein	NMB1672; NMC1590	No hints in the KEGG database (www.kegg.jp)	
NEIS1596	aromatic amino acid aminotransferase	NMB1678; NMC1596	Metabolic pathway	Biosynthesis of amino acids
NEIS1608	phosphoglucosamine mutase	NMB1690; NMC1608	Metabolism; Carbohydrate metabolism; Metabolic pathways; Biosynthesis of antibiotics	
NEIS1609	folP dihydropteroate synthase	NMB1691; NMC1609	Metabolic pathways; Metabolism of cofactors and vitamins	Folate biosynthesis
NEIS1619	rfaK alpha-1,2 N-acetylglucosamine transferase	NMB1705; NMC1619	Metabolism	Fatty acid metabolism
NEIS1622	putative integral membrane ion transporter	NMB1707; NMC1622	No hints in the KEGG database (www.kegg.jp)	
NEIS1655	GTP pyrophosphokinase	NMB1735; NMC1655	Metabolism; Nucleotide metabolism	Purine metabolism
NEIS1742	undecaprenyldiphospho-muramoylpentapeptide beta-N-acetylglucosaminyltransferase	NMB0422; NMC1742	Metabolism; Glycan biosynthesis and metabolism; Human Diseases; Drug resistance	Peptidoglycan biosynthesis; Vancomycin resistance
NEIS1747	phospho-N-acetylmuramoylpentapeptide- transferase	NMB0418; NMC1747	Metabolism; Glycan biosynthesis and metabolism; Human Diseases; Drug resistance	Peptidoglycan biosynthesis; Vancomycin resistance
NEIS1754	putative small periplasmic protein	NMB0412; NMC1754	No hints in the KEGG database (www.kegg.jp)	
NEIS1804	hypothetical periplasmic protein	NMB0366; NMC1804; NMV_0405	No hints in the KEGG database (www.kegg.jp)	
NEIS1808	ampG putative integral membrane signal transducer protein	NMB0360; NMC1808	Human diseases; Drug resistance	beta-Lactam resistance MFS transporter, PAT family, beta-lactamase induction signal transducer AmpG
NEIS1848	rpmA 50S ribosomal protein L27	NGO1677	Genetic information processing	
NEIS1849	hypothetical protein	NMB0323; NMC1849	No hints in the KEGG database (www.kegg.jp)	
NEIS1871	hypothetical protein	NGO1692; NMB0310; NMC1871	No hints in the KEGG database (www.kegg.jp)	

NEIS1872	hypothetical protein	NGO1693; NMB0309; NMC1872	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1873	dihydrofolate reductase	NMB0308; NMC1873	Metabolism; Metabolism of cofactors and vitamins	
NEIS1874	phospho-2-dehydro-3-deoxyheptonate aldolase	NMB0307; NMC1874	Metabolism; Biosynthesis of amino acids	
NEIS1875	hypothetical protein	NMB0306	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1876	hypothetical protein	Vide	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1877	opcB hypothetical protein		No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1927	cadmium resistance protein	NGO2127; NMB1955; NMC1927	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1929	acetyltransferase	NGO2125; NMB1957	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1930	putative periplasmic protein	NGO2124; NMB1958	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1933	periplasmic/outer membrane protein	NmB1961	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1934	hypothetical protein	Nmb1962; NmC1934	Environmental Information Processing; Membrane transport	ABC Transporter
NEIS1948	chaperonin GroEL	NGO2095; NMB1972; NMC1948	Genetic Information Processing; Folding, sorting and degradation	RNA degradation
NEIS1949	co-chaperonin GroES	NGO2094; NMB1973; NMC1949	Genetic Information Processing	
NEIS1951	putative sodium-dependent inner membrane transport protein	NGO2096; NMB1975; NMC1951	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1952	periplasmic/outer membrane protein	NGO2098; NMB1976; NMC1952	Metabolism; Amino acid metabolism	Biosynthesis of amino acids
NEIS1953	putative lipoprotein	NMB1977; NMC1953	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1964	putative membrane transport solute- binding protein	NMB1989; NMC1964	Environmental Information Processing; Membrane transport	ABC Transporter
NEIS1997	psedouridine synthase	NMB2018	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS1998	phosphopantetheine adenyltransferase	NGO2085; NMB2019; NMC1998	Metabolism; Metabolism of cofactors and vitamins	Metabolic pathways

NEIS2002	hypothetical protein	NMB2023; NMC2002	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS2017	tRNA pseudouridine synthase A	NGO1811; NMB2036; NMC2017	Genetic Information Processing; Translation	tRNA metabolism,
NEIS2022	hypothetical protein	NMB2041; NMC2022	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS2049	putative oxidoreductase	NMB2068; NMC2049	Metabolism; Metabolism of cofactors and vitamins	Thiamine metabolism
NEIS2081	elongation factor Ts	NMB2102; NMC2081	Genetic information processing	
NEIS2109	NHBA	NGO1958; NMB2132; NMC2109	Antigenic gene	
NEIS2113	putative periplasmic protein	NMB2135; NMC2113	No hints in the KEGG database ( <a href="http://www.kegg.jp">www.kegg.jp</a> )	
NEIS2134	rfaC Heptosyl transferase I	NMB2156; NMC2134	Metabolic pathways	Lipopolysaccharide biosynthesis
NEIS2153	6-phosphogluconate dehydrogenase	NMB0015; NMC2153	Metabolism; Carbohydrate metabolism	pentose phosphate pathway



**Supplementary figure. Neighbour-net phylogenetic network of the cultured isolates belonging to group C and clonal complex ST-11 from IMD cases with abdominal presentations.** The tree was performed on the basis of cgMLST. The groups are clustered in open circle according to the years of isolation.