1 Supplemental Materials

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3 Nanopore sequencing. Long-read genomic sequencing was performed using the third 4 generation Oxford Nanopore MinION Mklb (Isolates 1-30) and GridION X5 (Isolates 31-40; 5 Oxford, England) sequencing instruments. Genomic DNA was extracted from pure cultures 6 using the DNeasy PowerBiofilm Kit (Qiagen, Hilden, Germany). Each Nanopore sequencing 7 library was prepared using 5 µg of DNA with the 1D ligation kit (SQK-LSK108, Oxford Nanopore 8 Technologies) using R9.4 flowcells (FLO-MIN106). A single isolate was run per flowcell. 9 MinKNOW software was used to collect sequencing data. Three separate analysis pipelines 10 were performed: (1) a real-time Nanopore analysis approach, (2) an assembly-based Nanopore approach, and (3) an Illumina Pilon-corrected approach. The run statistics and the whole 11 genome assembly parameters are summarized in the Supplemental File Run & Assembly 12 13 Statistics. Sequencing data for this study were deposited in the Sequencing Read Archive (SRA; BioProject number: PRJNA496461), and genome assemblies submitted to NCBI. 14

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Nanopore real-time approach. For the real-time analysis approach, the Oxford Nanopore Technology "What's In My Pot" (WIMP)(1) and Metrichor's Antimicrobial Resistance Mapping Application (ARMA) (2) real-time analysis tools were run in parallel to both sequencing and base-calling. WIMP uses a customized pipeline applying the Centrifuge metagenomic classifier to the sequencing reads. ARMA aligns sequencing reads to the Comprehensive Antimicrobial Database (CARD)(3), identifying antimicrobial resistance (AMR) gene hits.

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Nanopore assembly-based approach. For the assembly-based approach, Albacore v2.1.3
was used to base-call. Raw data were corrected, trimmed, and assembled using Canu v1.6(4)
using default parameters. Genome size was assumed to be 5.3Mb. For isolates that did not
assemble under default parameters, either read quality restrictions were relaxed or minimum

overlap requirements were shortened as suggested by the software documentation. Assembled
contigs were screened for resistance genes using Abricate

(htts://github.com/tseemann/abricate), a tool that uses alignment to search for resistance gene
sequences from several database including ResFinder, CARD, ARG-ANNOT, and the NCMI
AMR Reference Gene Database. ResFinder results were evaluated in this study(5). In a
separate experiment, we were able to build high quality genomes from nanopore electrical data
in under 6 hours using a machine with 36 cores and 72GB RAM. Thirteen random blocks of
4000 reads were sampled and taken through basecalling, assembly and polishing.
Conservatively, it takes at most an hour to reach 52,000 reads on a typical run.

Illumina sequencing. WGS was also conducted using Illumina MiSeg short-read sequencing to 37 increase assembly accuracy (Illumina, San Diego, California). A drawback with Illumina 38 39 sequencing is the turn-around time as sequencing alone requires between 19-24 hours for 300 40 cycles. As the ultimate goal would be to use Nanopore sequencing alone for both resistance gene and chromosomal mutation identification, in the current analysis, the Pilon-corrected 41 42 assemblies were not meant to supplant or supplement Nanopore sequencing but rather to serve 43 as a reference standard to determine the accuracy of Nanopore sequencing results. Approximately 100-500 ng of gDNA was used to prepare sequencing libraries using the Nextera 44 Flex Kit. The each Illumina library was then sequenced using both v2 2x150 and v3 2x75 45 46 reagents on an Illumina Miseq. These reads were used to correct the more error prone Nanopore assembly with the Pilon v1.22 software package in conjunction with the short-read 47 aligner Bowtie2 v2.2.6. 48

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Analysis for Detection of Chromosomal Mutations. Both Nanopolished Nanopore
 assemblies and hybrid Illumina-corrected Nanopore assemblies were further evaluated for
 chromosomal mutations presumed to confer resistance. These included truncations in the outer

membrane proteins OmpK35 and OmpK36 as a consequence of premature stop codons
resulting in carbapenem resistance and *gyrA* (DNA gyrase; nucleotide positions 247-249 & 259261) and *parC* (topoisomerase IV; nucleotide positions 238-240 & 250-252) point mutations that
encoded amino acid changes resulting in fluoroquinolone resistance. Additionally, mutations in *mgrB*, the negative regulator of the two-component regulatory system that renders polymixins
ineffective were evaluated.

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60 Coding sequences encompassing chromosomal mutations of interest were extracted from the 61 genome of the K. pneumoniae ATCC 13883 strain and used to align with genomic assemblies using minimap2 (6). Code written in C++ was developed for parsing alignment data and 62 mutations, evaluating their impact on amino acid translation based on resulting codon 63 64 changes(7). Substitutions causing synonymous codons were reported as such, and frameshift 65 mutations were followed downstream to report premature stop codons. Additionally, the program analyzed DNA sequences surrounding mutation sites looking for homopolymers or 66 methylation motifs specific for K. pneumoniae as indicators of potential sequencing issues 67 rather than mutations in the genome. 68

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Predicted correlations between resistance genes/mutations and AST results. Predictions 70 71 of resistance were performed without reference to phenotypic data. The correlation of resistance genes and sequence variants with anticipated AST results for the evaluated antibiotics was 72 73 determined based on reference gene databases and the published literature(8-26). For associations for which ambiguity existed, the following rules were established a priori: 74 SHV 2be extended-spectrum β-lactamase enzymes were assumed to inactivate 75 ceftriaxone and cefepime if they contained G238S or E240K mutations(19, 27) 76 The relative contributions of porins OmpK35 and/or OmpK36 truncations to β-lactam 77 • resistance have not been well established (13, 28-32). There appears to be consensus 78

79	that when premature stop codons are present for both, in conjunction with ESBLs or
80	AmpC cephalosporinases, carbapenem resistance is likely.
81	Aminoglycoside modifying enzymes (AMEs)- including aminoglycoside N-
82	acetyltransferases [AACs], aminoglycoside O-nucleotidyltransferases [ANTs], or
83	aminoglycoside O-phosphotransferases [APHs] are anticipated to confer resistance to
84	gentamicin and tobramycin (17). Correlations between the number of different enzymes
85	produced and the association with aminoglycoside resistance are not well defined. After
86	exploratory analysis (Table 1), we predicted that when four or more AMEs were present,
87	gentamicin and tobramycin resistance was likely.
88	• The AME aac(6')Ib-cr was also evaluated for its contribution to ciprofloxacin
89	resistance(17).
90	• Ribosomal RNA methyltransferases (armA, rmtA, rmtB, rmtC, rmtD, or rmtE) are
91	expected to confer resistance to amikacin, gentamicin, and tobramycin (18).
92	• Plasmid-encoded quinolone resistance genes qnrB, qnrS, aac(6')Ib-cr and oqxAB
93	(chromosomally encoded) were predicted to cause low-level fluoroquinolone resistance,
94	but not frank resistance (16, 33, 34).
95	Single gyrA or parC mutations were not predicted to cause fluoroquinolone resistance but two-
96	step gyrA mutations or the presence of both gyrA and parC mutations translating to amino acid
97	changes were expected to result in fluoroquinolone resistance (33, 34).
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Supplemental Table 1: Anticipated antibiotic susceptibility results for 40 *Klebsiella pneumoniae* isolates based on resistance determinants detected by Nanopore sequencing technology real-time analysis; first column for each antibiotic indicates presumed activity and second column for each antibiotic indicates *in vitro* activity based on broth microdilution results with green indicating susceptible and red indicating intermediate or resistant; number on bottom represents percent agreement between presumed and *in vitro* activity

#	Resistance determinants identified with real-time Nanopore [# of allelic variants identified for each gene]*	Missing resistance determinants based on pilon- corrected Illumina data	Piperad tazoba	actam	Ceftr	iaxone	Cefe	pime	Ertap	enem	Meroj	benem	Amik	acin	Genta	imicin	Ciprof	loxacin	Colis	stin	Doxy	cycline	TM SM	IP- 1X
1	bla _{SHV} [75]; bla _{CTX-} _M [34]; bla _{OXA} [2]; bla _{KPC} [18]; aac[7]; qnr[6]; oqxA[1]; oqxB[1]; aadA[4]; su[1]]; dfr[1]	Two-step <i>gyrA</i> mutations; OmpK36 truncation																						
2	bla _{SHV} [81] (bla _{LEN}); bla _{CTX-M} [31]; bla _{OXA} [2]; bla _{TEM} [104]; bla _{KPC} [11]; qnr[7]; aac[13]; aadA[9]; dfr[1]	oqxA; oqxB; tet(B); aph(6")- Id; aph(3')-la; sul1; sul2; one- step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation																						
3	bla _{SHV} [25]; oqxA[1]; oqxB[1]	OmpK36 truncation																						
4	bla _{SHV} [57]; bla _{TEM} [48]; bla _{KPC} [4]; aadA[4]	oqxA; oqxB; sul1; one-step gyrA mutation, parC mutation; OmpK36 truncation																						
5	bla _{SHV} [70]; oqxA[1]; oqxB[1]	OmpK36 truncation																						

6	bla _{SHV} [5]; bla _{TEM} [1]; bla _{OXA} [2]; bla _{KPC} [14]; aac[3]; oqxA[1]; oqxB[1]; aph[2]; aadA[1]; sul[1]; dfr[1]	two-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation											
7	bla _{OXA} [4]; bla _{SHV} [19]; oqxA[1]; oqxB[1]; aac[1]; aadA[3]; sul[1]; dfr[1]	two-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation											
8	bla _{OXA} [2]; bla _{TEM} [3]; bla _{CTX} . _M [27]; bla _{SHV} [30]; aac[6]; oqxA; oqxB; qnr[12]; aph[2]; sul[2]; dfr[1]; tet[1]	one-step gyrA mutation; parC mutation; aacA4; OmpK36 truncation											
9	$bla_{SHV}(bla_{LEN})[94]$	oqxA; oqxB											-
10	bla _{OXA} [3]; bla _{CTX} . _M [31]; bla _{TEM} [6]; bla _{SHV} [57]; aac[7]; qnr[21]; oqxA[1]; oqxB[1]; aph[2]; su[2]; dfr[1]; tet[1]	OmpK36 truncation											
11	bla _{CTX-M} [18]; bla _{TEM} [15]; bla _{SHV} [56]; aac[3]	oqxA; oqxB; sul2; dfrA14; aph(6)-ld; aph(3")-lb; OmpK36 truncation											
12	bla _{TEM} [58]; bla _{SHV} [32]; bla _{CTX} . _M [6]; bla _{NDM} [5]; bla _{OXA} [2]; qnr[13]; aac[8]; aph[1]; aadA[3]	rmtf; oqxA; oqxB; OmpK35 truncation; sul1; dfrA12; one- step gyrA mutation; parC mutation											

13	bla _{OXA} [2]; bla _{CTX-} _M [7]; bla _{TEM} [1]; bla _{SHV} [8]; bla _{NDM} [6]; qnr[1]; oqxA[1]; oqxB[1]; aadA[1]; aac[2]; sul[1]	OmpK35 and OmpK36 truncation; one- step gyrA mutation; parC mutation											
14	bla _{SHV} [89]; bla _{OXA} [3]; bla _{TEM} [18]; bla _{CTX-} _M [23]; bla _{KPC} [18]; aac[20]; aadA[10]; tet[4]; dfrA[1]; sul[2]	oqxA; oqxB; tet(B); aph(6)-Id; aph(3")-Ib; one- step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation											
15	bla _{SHV} [87]; oqxA[1]; oqxB[1]; qnr[6]; sul[1]; dfr[1]; tet[1]	<i>tet(A); tet(D);</i> OmpK36 truncation; <i>mgrB</i> mutation											
16	bla _{SHV} [116]; bla _{KPC} [18]; aac[17]; oqxA[1]; oqxB[1]; aadA[9]; aac[18]; sul[1]	two-step gyrA mutations; parC mutation; Ompk35 and Ompk36 truncation											
17	bla _{CTX-M} [42]; bla _{KPC} [18]; bla _{SHV} [62]; bla _{TEM} [23]; bla _{OXA} [22]; oqxA[1]; oqxB; aac[22]; aph[9]; tet[1]; sul[3] dfr[4]	two-step <i>gyrA</i> mutations; OmpK36 truncation											
18	bla _{CTX-M} [23]; bla _{TEM} [36]; bla _{KPC} [8]; bla _{SHV}	oqxA; oqxB; tet(A); two-step gyrA mutation; parC mutation; OmpK36 truncation											

19	bla _{TEM} [20]; bla _{SHV} [52]; bla _{OXA} [1]; bla _{KPC} [1]; qnr[1]; aac[2]; aadA[3]	oqxA; oqxB; OmpK36 truncation; one- step gyrA mutation; parC mutation; dfrA14											
20	bla _{SHV} [108]; bla _{TEM} [111]; bla _{KPC} [11]; aac[13]; aadA[10]	bla _{0XA-9} ; oqxA; oqxB; one-step gyrA mutation; parC mutation; OmpK35 mutation; OmpK36 truncation; aph(3')-la; aph(4)-la; sul1; dfrA12											
21	bla _{KPC} [18]; bla _{SHV} [98]; bla _{TEM} [21]; aac[17]; aadA[8]; oqxA[1]; oqxB[1]; sul[1]; dfrA[1]	one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation											
22	bla _{TEM} [22]; bla _{KPC} [18]; bla _{OXA} [1]; bla _{SHV} [41]; qnr[10]; oqxA[1]; oqxB[1]; aac[9]; aadA[5]	one-step gyrA mutation; parC mutation; mgrB mutation; OmpK36 truncation											
23	bla _{KPC} [16]; bla _{SHV} [56]; bla _{OXA} [2]; bla _{TEM} [8]; aac[15]; oqxA; oqxB; aph[1]; aadA[7]; sul[2]; dfrA[1]	one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation											
24	bla _{TEM} [64]; bla _{CTX} . _M [35]; bla _{DHA} [6]; bla _{SHV} [67]; qnr[1]; aac[1]; aadA[7]	rmtB; oqxA; oqxB; one-step gyrA mutation; OmpK36											

		truncation; tet(A); tet(G); aph(3')-la; aph(3'')-lb; aph(3)-lld; aph(6)-ld; sul1; sul2; dfrA12; dfrA1											
25	bla _{SHV} [72]; oqxA[1]; oqxB[1]	OmpK36 truncation											
26	bla _{SHV} [68]; bla _{KPC} [18]; oqxA[1]; oqxB[1]; aac[11]; aadA[8]	One-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation											
27	bla _{SHV} [59]; bla _{TEM} [41]; bla _{KPC} [6]; aac[8]; aadA[5]	bla _{OXA} ; oxqA; oqxB; OmpK35 and OmpK36 truncation; aph(3')-la; one- step gyrA mutation; parC mutation; sul1; dfrA12											
28	bla _{SHV} [94]; bla _{TEM} [14]; bla _{OXA} [2]; bla _{KPC} [18]; aac[14]; oqxA[1]; oqxB[1]; aph[2]; aad[5]; sul[2]; dfrA[1]	one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation; premature stop codon in mgrB											
29	bla _{SHV} [29]; bla _{NDM} [7]; bla _{CTX-} _M [22]; bla _{CMY} [39]; qnr[12]; aac[10]; aadA[5]; sul[1]	rmtf; oqxA; oqxB; one-step gyrA mutation; parC mutation; OmpK35 truncation; aacA4; aph(3')- Vla; dfrA12											

30	bla _{SHV} [45]; bla _{TEM} [38]; bla _{OXA} [6]; bla _{KPC} [9]; aac[2]; aadA[5];	oqxA; oqxB; qnrS1; two-step gyrA mutation; parC mutation; phoP mutation; OmpK36 truncation; aph(3')-la; sul1; sul3; dfrA12											
31	bla _{CTX-M} [19]; bla _{TEM} [22]; bla _{SHV} [36]; qnr[11]	oqxA; oqxB; OmpK36 truncation; aph(6)-Id; aph(3")-Ib; sul2; dfrA14											
32	bla _{OXA} [3]; bla _{SHV} [60]; bla _{CTX-} м[23]; bla _{TEM} [20]; qnr[12]; aac[2]	oqxA; oqxB; tet(A); aph(6)- ld; aph(3")-lb; sul2; dfrA14; OmpK36 truncation											
33	bla _{SHV} [25](bla _{LEN} [2 5]; oqxA[1]; oqxB[1]; sul2[1]; dfrA14[1]	OmpK36 truncation; <i>tet(D)</i>											
34	bla _{SHV} [23]; oqxA[1]; oqxB[1]	OmpK36 truncation											
35	bla _{SHV} [24]; oqxA[1]; oqxB[1]	OmpK36 truncation											
36	bla _{SHV} [22]; oqxA[1]; oqxB[1]	ant(2")-la; OmpK36 truncation											
37	bla _{TEM} [41]; bla _{KPC} [8]; bla _{SHV} [85]; ant[1]	<i>qnrS1;</i> OmpK36 truncation											
38	bla _{OKP} [9]; bla _{TEM} [12]; bla _{SHV} [1]; oqxA; oqxB; sul; dfr	<i>tet(D);</i> OmpK36 truncation											

39	bla _{SHV} [62]; oqxA[1]; oqxB[1]	OmpK36 truncation											
40	bla _{SHV} [23]; oqxA[1]; oqxB[1]	OmpK36 truncation											
	Overall agre	ement	80%	93%	95%	83%	93%	78%	45%	30%	93%	63%	68%

*Due to the raw sequencing error rate for the real-time Nanopore sequencing analysis, multiple variants of resistance genes are frequently identified by ARMA. For example, for the result "*bla*_{KPC}[3]," three allelic variants would be identified *bla*_{KPC-2}, *bla*_{KPC-3}, *bla*_{KPC-5}.

Supplemental Table 2: Anticipated antibiotic susceptibility results for 40 *Klebsiella pneumoniae* isolates based on resistance determinants detected by Nanopore sequencing technology with assembly; first column for each antibiotic indicates presumed activity and second column for each antibiotic indicates *in vitro* activity based on broth microdilution results with green indicating susceptible and red indicating intermediate or resistant; number on bottom represents percent agreement between presumed and *in vitro* activity

#	Resistance determinants identified with Nanopore sequencing with assembly	Missing resistance determinants based on pilon- corrected Illumina data	Piperacillin- tazobactam	Ceftriaxor	e Cefepim	e Ertapenem	Meropenem	Amikacin	Gentamicin	Ciprofloxacin	Colistin	Doxycycline	TMP- SMX
1	bla _{SHV-1} ; bla _{CTX-M-15} ; bla _{OXA-1} ; bla _{KPC-3} ; OmpK36 truncation; qnrS1; oqxA; oqxB; two-step gyrA mutations; aac(6')- lb-cr; aadA2; sul1; dfrA12	None											
2	bla _{SHV-11} ; bla _{CTX-M-15} ; bla _{OXA-1} ; bla _{TEM-1} ; bla _{KPC-2} ; OmpK35 and OmpK36 truncation; qnrB1; oqxA; oqxB; one-step gyrA mutation; parC mutation; tet(B); aadA2; aph(3')-la; aac(3)-lld; aac(6')-lb- cr; aadA2; aac(3)-lla; aph(6'')-ld; aaA1; aac(6')-lb; sul1; sul2; dfrA12; dfrA30	None											
3	<i>bla</i> _{SHV-11} ; <i>oqxA</i> ; <i>oqxB</i> ; Ompk36 truncation	None											
4	bla _{SHV-11} ; bla _{TEM-1} ; bla _{KPC-3} ; OmpK36 truncation; oqxA; oqxB; one-step gyrA	None											

								 _	_		_		_	_
	mutation; <i>parC</i> mutation; <i>aadA2</i> ; <i>sul1</i>													
5	<i>bla</i> _{SHV-11} ; Ompk36 truncation; <i>oqxA</i> ; <i>oqxB</i>	None												
6	bla _{SHV-11} ; bla _{TEM-1} ; bla _{OXA-9} ; bla _{KPC-3} ; aac(6')-lb-cr; oqxA; oqxB; two-step gyrA mutations; parC mutation; ompK35 and OmpK36 truncation; aph(3")- lb; aph(6)-ld; aadA1; aac(6)-lb; sul2; dfrA14	None												
7	bla _{OXA-2} ; bla _{SHV-11} ; bla _{SHV-30} ; bla _{SHV-12} ; oqxA; oqxB; aac(6')- lb-cr; two-step gyrA mutations; parC mutation; OmpK35 and Ompk36 truncation; aadA2; aacA4; sul1; dfrA12; fosA	None												
8	bla _{OXA-1} ; bla _{TEM-1} ; bla _{CTX-M-15} ; bla _{SHV-28} ; OmpK36 truncation; aac(6')-lb-cr; oqxA; oqxB; qnrB1; one- step gyrA mutation; parC mutation; tet(A); aph(3")-lb; aph(6)-ld; aac(3)-lla; sul2; dfrA14	bla _{OXA-47} ; aacA4												
9	bla _{LEN-12} ; bla _{SHV-11} ; OmpK36 truncation; oqxA; oqxB	None												

10	bla _{OXA-1} ; bla _{CTX-M-15} ; bla _{TEM-1} ; bla _{SHV-101} ; OmpK36 truncation; aac(6')-lb-cr; qnrB1; oqxA; oqxB; tet(A); aac(3)-lla; aac(6)-ld; aac(3")-lb; aph(6)-ld; aph(3")-lb	aacA4											
11	bla _{CTX-M-15} ; bla _{TEM-1} ; bla _{SHV-11} ; OmpK36 truncation; aac(6')- lb-cr; oqxA; oqxB; aph(6)-ld; aph(3")-lb; sul2; dfrA14	None											
12	bla _{TEM-1} ; bla _{SHV-1} ; bla _{CTX-M-15} ; bla _{NDM-1} ; bla _{OXA-48} ; OmpK35 truncation; qnrB1; rmtf; aac(6')-lb-cr; aph(3')-Vla; oqxA; oqxB; one-step gyrA mutation, parC mutation; sul1; dfrA12	None											
13	bla _{OXA-1} ; bla _{CTX-M-15} ; bla _{TEM-1} ; bla _{SHV-11} ; bla _{OXA-9} ; bla _{NDM-1} ; aac(6')-lb-cr; qnrS1; oqxA; oqxB; one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation; aadA1; aac(6')-lb; sul1	None											
14	bla _{SHV-11} ; bla _{SHV-2} ; bla _{OXA-1} ; bla _{TEM-1} ; bla _{CTX-M-15} ; bla _{KPC-2} ; oqxA; oqxB; aac(6')- lb-cr; aac(6')-lb; aph(3')-la; aadA1; aadA2; aac(3)-lld;	None											

	aac(6')-Ib-cr; aac(3')- Ila; aph(6)-Id; aph(3")-Ib; one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation; tet(B); sul2; dfrA30												
15	bla _{SHV-11} ; bla _{SHV-1} ; OmpK36 truncation; oqxA; oqxB; qnrB2; mgrB mutation; tet(A); tet(D); sul1; dfrA25	None											
16	bla _{SHV-11} ; bla _{KPC-3} ; bla _{SHV-12} ; aac(6')-lb- cr; oqxA; <i>oqxB</i> ; two- step <i>gyrA</i> mutations; <i>parC</i> mutation; OmpK35 and OmpK36 truncation; <i>aadA2</i> ; <i>aadA1</i> ; <i>aac(6')-lb; sul3</i>	bla _{KPC-9}											
17	<i>bla</i> _{CTX-M-15} ; <i>bla</i> _{KPC-2} ; <i>bla</i> _{SHV-28} ; <i>bla</i> _{TEM-1B} ; <i>bla</i> _{OXA-1} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i> ; aac(6')-lb-cr; two-step <i>gyrA</i> mutations; <i>aph(3")</i> - <i>lb</i> ; <i>aph(6)-ld</i> ; <i>aac(3)</i> - <i>lla</i> ; <i>tet(A)</i> ; <i>sul2</i> ; <i>dfrA14</i>	None											
18	bla _{CTX-M-15} ; bla _{TEM-1B} ; bla _{KPC-2} ; bla _{SHV-28} ; OmpK36 truncation; oqxA; oqxB; one-step gyrA mutation; parC mutation; tet(A)	One-step gyrA mutation											
19	bla _{кPC-3} ; bla _{TEM-1} ; bla _{OXA-9} ; bla _{SHV-11} ;												

	oqxA; oqxB; qnrS1; aac(6')-lb-cr; one- step gyrA mutation; parC mutation; aadA1; aac(6')-lb; OmpK36 truncation; dfrA14												
20	bla _{SHV-11} ; bla _{OXA-9} ; bla _{KPC-2} ; bla _{TEM-1} ; OmpK35 and OmpK36 truncation; aac(6')-lb-cr; oqxA; oqxB; one-step gyrA mutation; aph(3')-la; aadA2; aadA1; aac(6')-lb; aac(3)- IVa; aph(4)-la; aadA15; sul1; dfrA12	None											
21	bla _{KPC-3} ; bla _{SHV-12} ; bla _{TEM-1} ; bla _{SHV-11} ; OmpK35 and OmpK36 truncation; aac(6')-lb-cr; oqxA; oqxB; one-step gyrA mutation; parC mutation; aadA2; aac(6')-lb; sul1; dfrA12	None											
22	bla _{TEM-1} ; bla _{KPC-3} ; bla _{OXA-9} ; bla _{SHV-11} ; OmpK36 truncation; qnrB19; oqxA; oqxB; aac(6')-lb-cr; one- step gyrA mutation; parC mutation; mgrB mutation; aac(3)-lld; aac(6')-lb; aadA1	None											
23	bla _{KPC-2} ; bla _{SHV-11} ; bla _{OXA-9} ; bla _{TEM-1} ; aac(6')-Ib-cr; oqxA;	None											

	oqxB; one-step gyrA mutation; parC mutation; OmpK35 and Ompk36 truncation; aac(6')- lb; aadA2; aac(3)-IVa; aph(4)-la; aadA2; aadA1; sul1; sul3; dfrA12												
24	bla _{TEM-1} ; bla _{CTX-M-14} ; bla _{DHA-1} ; bla _{SHV-11} ; OmpK36 truncation; qnrB4; oqxA; oqxB; one-step gyrA mutation; tet(A); tet(G); rmtB; aph(3")- lb; aph(3')-la; aac(3)- lld; aph(6)-ld; aph(3)- lld; aadA2; aadA5; sul1; sul2; dfrA12; dfrA1	None											
25	<i>bla</i> _{SHV-11} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>	None											
26	bla _{SHV-11} ; bla _{KPC-2} ; oqxA; oqxB; one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation; aac(6')- lb; aadA2; aadA1; aadA24	None											
27	bla _{SHV-11} ; bla _{TEM-1} ; bla _{OXA-9} ; bla _{KPC-2} ; oqxA; oqxB; aac(6')- lb-cr; one-step gyrA mutation; parC mutation; aph(3')-la; aadA2; aac(6')-lb; sul1; dfrA12	None											

28	bla _{SHV-12} ; bla _{TEM-1} ; bla _{OXA-9} ; bla _{KPC-3} ; bla _{SHV-11} ; OmpK35 and OmpK36 truncation; aac(6')- lb-cr; oqxA; oqxB; one-step gyrA mutation; parC mutation; aac(6')-lb; aph(3")-lb; aadA1; sul2; dfrA14; premature stop codon in mgrB	None											
29	bla _{SHV-1} ; bla _{NDM-1} ; bla _{CTX-M-15} ; bla _{CMY-4} ; OmpK35 truncation; qnrB1; aac(6')-lb-cr; oqxA; oqxB; one-step gyrA mutation; parC mutation; rmtf; aacA4; aph(3')-Vla; aadA2; sul1; dfrA12	None											
30	bla _{SHV-11} ; bla _{TEM-1} ; bla _{OXA-2} ; bla _{KPC-3} ; OmpK36 truncation; <i>phoP</i> mutation; <i>aac(6')-lb-cr; oqxA</i> ; <i>oqxB</i> ; <i>qnrS1</i> ; two- step <i>gyrA</i> mutation; <i>parC</i> mutation; <i>aadA8b; aadA1;</i> <i>aadA2; aac(3)-lla;</i> <i>aacA4; aph(3')-la;</i> <i>sul1; sul3; dfrA12</i>	aadA8											
31	bla _{CTX-M-15} ; bla _{TEM-1} ; bla _{SHV-83} ; OmpK36 truncation; oqxA; oqxB; qnrB1; aph(6)- ld; aph(3")-lb; sul2; dfrA14												

32	bla _{OXA-1} ; bla _{SHV-11} ; bla _{CTX-M-15} ; bla _{TEM-1B} ; OmpK36 truncation; oqxA; oqxB; qnrB1; aac(6')-lb-cr; tet(A); aph(6)-ld; aph(3'')-lb; sul2; dfrA14																							
33	bla _{LEN-12} ; bla _{SHV-1} ; OmpK36 truncation; oqxA; oqxB; tet(D); sul2; dfrA14	None																						
34	<i>bla</i> _{SHV-71} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>	None																						
35	<i>bla</i> _{SHV-1} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>	None																						
36	<i>bla</i> _{SHV-36} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i> ; <i>ant(2″)-la</i>	None																						
37	bla _{TEM-1} ; bla _{KPC-3} ; bla _{SHV-26} ; bla _{SHV-30} ; OmpK36 truncation; ant(2")-la; qnrS1	None																						
38	bla _{OKP-B2} ; bla _{TEM-1} ; bla _{SHV-122} ; OmpK36 truncation; oqxA; oqxB; tet(D); sul2; dfrA26	None																						
39	<i>bla</i> _{SHV-62} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>	None																						
40	<i>bla</i> _{SHV-83} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>	None																						
	Overall agreer	nent	8	5%	9	5%	9	8%	85	5%	95	5%	85	%	93	8%	98	3%	98	%	8	0%	93	%

Supplemental Table 3: Anticipated antibiotic susceptibility results for 40 *Klebsiella pneumoniae* isolates based on resistance determinants detected by Nanopore sequencing technology with assembly and Pilon-corrected Illumina data; first column for each antibiotic indicates presumed activity and second column for each antibiotic indicates *in vitro* activity based on broth microdilution results with green indicating susceptible and red indicating non-susceptible; number on bottom represents percent agreement between presumed and *in vitro* activity

#	Resistance mechanisms identified	Piper tazol	racillin- bactam	Ceftriaxone	Cef	epime	Ertapene	em	Merope	enem	Amik	acin	Genta	micin	Ciprofl	oxacin	Coli	stin	Doxy	cycline	TN SN	1Р- ЛХ
1	bla _{SHV-1} ; bla _{CTX-M-15} ; bla _{OXA-1} ; bla _{KPC-3} ; OmpK36 truncation; qnrS1; oqxA; oqxB; two-step gyrA mutations; aac(6')-lb-cr; aadA2; sul1; dfrA12																					
2	bla _{SHV-11} ; bla _{CTX-M-15} ; bla _{OXA-1} ; bla _{TEM-1} ; bla _{KPC-2} ; OmpK35 and OmpK36 truncation; qnrB1; oqxA; oqxB; one- step gyrA mutation; parC mutation; tet(B); aadA2; aph(3')-la; aac(3)-lld; aac(6')-lb-cr; aadA2; aac(3)-lla; aph(6'')-ld; aaA1; aac(6')-lb; sul1; sul2; dfrA12; dfrA30																					
3	<i>bla</i> _{SHV-11} ; <i>oqxA</i> ; <i>oqxB</i> ; OmpK36 truncation																					
4	<i>bla</i> _{SHV-11} ; <i>bla</i> _{TEM-1} ; <i>bla</i> _{KPC-3} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i> ; one-step <i>gyrA</i> mutation; <i>parC</i> mutation; <i>aadA2</i> ; <i>sul1</i>																					
5	<i>bla</i> _{SHV-11} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>																					
6	bla _{SHV-11} ; bla _{TEM-1} ; bla _{OXA-9} ; bla _{KPC-3} ; aac(6')- <i>lb</i> -cr; oqxA; oqxB; two-step gyrA mutations; parC mutation; OmpK35 and OmpK36 truncation; aph(3")- <i>lb</i> ; aph(6)- <i>ld</i> ; aadA1; aac(6)- <i>lb</i> ; sul2; dfrA14																					
7	bla _{OXA-2} ; bla _{SHV-11} ; bla _{SHV-30} ; bla _{SHV-12} ; oqxA; oqxB; aac(6')-Ib-cr; two-step gyrA mutations; parC mutation; OmpK35 and OmpK36 truncation; aadA2; aacA4; sul1; dfrA12; fosA																					
8	bla _{OXA-1} ; bla _{OXA-47} ; bla _{TEM-1} ; bla _{CTX-M-15} ; bla _{SHV-28} ; OmpK36 truncation; aac(6')-																					

	<i>lb-cr; oqxA; oqxB; qnrB1; one-step</i> <i>gyrA</i> mutation; <i>parC</i> mutation; <i>tet(A);</i> <i>aph(3")-lb; aph(6)-ld; aac(3)-lla;</i> aacA4; <i>sul2; dfrA14</i>											
9	<i>bla</i> _{LEN-12} ; <i>bla</i> _{SHV-11} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>											
10	bla _{OXA-1} ; bla _{CTX-M-15} ; bla _{TEM-1} ; bla _{SHV-101} ; OmpK36 truncation; aac(6')-lb-cr; qnrB1; oqxA; oqxB; tet(A); aacA4; aac(3)-lla; aac(6)-ld; aac(3")-lb; aph(6)-ld; aph(3")-lb											
11	bla _{CTX-M-15} ; bla _{TEM-1} ; bla _{SHV-11} ; OmpK36 truncation; aac(6')-lb-cr; oqxA; oqxB; aph(6)-ld; aph(3")-lb; sul2; dfrA14											
12	bla _{TEM-1} ; bla _{SHV-1} ; bla _{CTX-M-15} ; bla _{NDM-1} ; bla _{OXA-48} ; OmpK35 truncation; qnrB1; rmtf; aac(6')-lb-cr; aph(3')-Vla; oqxA; oqxB; one-step gyrA mutation, parC mutation; sul1; dfrA12											
13	bla _{OXA-1} ; bla _{CTX-M-15} ; bla _{TEM-1} ; bla _{SHV-11} ; bla _{OXA-9} ; bla _{NDM-1} ; aac(6')-lb-cr; qnrS1; oqxA; oqxB; one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation; aadA1; aac(6')-lb; sul1											
14	bla _{SHV-11} ; bla _{SHV-2} ; bla _{OXA-1} ; bla _{TEM-1} ; bla _{CTX-M-15} ; bla _{KPC-2} ; oqxA; oqxB; aac(6')-lb-cr; aac(6')-lb; aph(3')-la; aadA1; aadA2; aac(3)-lld; aac(6')-lb- cr; aac(3')-lla; aph(6)-ld; aph(3'')-lb; one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation; tet(B); sul2; dfrA30											
15	<pre>bla_{SHV-11}; bla_{SHV-1}; OmpK36 truncation; oqxA; oqxB; qnrB2; mgrB mutation; tet(A); tet(D); sul1; dfrA25</pre>											
16	bla _{SHV-11} ; bla _{KPC-3} ; bla _{KPC-9} ; bla _{SHV-12} ; aac(6')-lb-cr; oqxA; oqxB; two-step gyrA mutations; parC mutation; OmpK35 and OmpK36 truncation; aadA2; aadA1; aac(6')-lb; sul3											

17	bla _{CTX-M-15} ; bla _{KPC-2} ; bla _{SHV-28} ; bla _{TEM-1B} ; bla _{OXA-1} ; OmpK36 truncation; oqxA; oqxB; aac(6')-lb-cr; two-step gyrA mutations; aph(3")-lb; aph(6)-ld; aac(3)-lla; tet(A); sul2; dfrA14											
18	bla _{CTX-M-15} ; bla _{TEM-1B} ; bla _{KPC-2} ; bla _{SHV-28} ; OmpK36 truncation; oqxA; oqxB; two- step gyrA mutations; parC mutation; tet(A)											
19	bla _{KPC-3} ; bla _{TEM-1} ; bla _{OXA-9} ; bla _{SHV-11} ; oqxA; oqxB; qnrS1; aac(6')-lb-cr; one- step gyrA mutation; parC mutation; aadA1; aac(6')-lb; dfrA14; OmpK36 truncation											
20	bla _{SHV-11} ; bla _{OXA-9} ; bla _{KPC-2} ; bla _{TEM-1} ; OmpK35 and OmpK36 truncation; aac(6')-lb-cr; oqxA; oqxB; one-step gyrA mutation; parC mutation; aph(3')-la; aadA2; aadA1; aac(6')-lb; aac(3)-lVa; aph(4)-la; aadA15; sul1; dfrA12											
21	bla _{KPC-3} ; bla _{SHV-12} ; bla _{TEM-1} ; bla _{SHV-11} ; OmpK35 and OmpK36 truncation; aac(6')-lb-cr; oqxA; oqxB; one-step gyrA mutation; parC mutation; aadA2; aac(6')-lb; sul1; dfrA12											
22	bla _{TEM-1} ; bla _{KPC-3} ; bla _{OXA-9} ; bla _{SHV-11} ; OmpK36 truncation; qnrB19; oqxA; oqxB; aac(6')-lb-cr; one-step gyrA mutation; parC mutation; mgrB mutation; aac(3)-lld; aac(6')-lb; aadA1											
23	bla _{KPC-2} ; bla _{SHV-11} ; bla _{OXA-9} ; bla _{TEM-1} ; aac(6')-lb-cr; oqxA; oqxB; one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation; aac(6')-lb; aadA2; aac(3)-IVa; aph(4)- la; aadA2; aadA1; sul1; sul3; dfrA12											
24	<pre>bla_{TEM-1}; bla_{CTX-M-14}; bla_{DHA-1}; bla_{SHV-11}; OmpK36 truncation; qnrB4; oqxA; oqxB; one-step gyrA mutation; tet(A);</pre>											

	tet(G); rmtB; aph(3″)-Ib; aph(3′)-Ia; aac(3)-IId; aph(6)-Id; aph(3)-IId; aadA2; aadA5sul1; sul2; dfrA12; dfrA1											
25	<i>bla</i> _{SHV-11} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>											
26	bla _{SHV-11} ; bla _{KPC-2} ; oqxA; oqxB; one-step gyrA mutation; parC mutation; OmpK35 and OmpK36 truncation; aac(6')-lb; aadA2; aadA1; aadA24											
27	bla _{SHV-11} ; bla _{TEM-1} ; bla _{OXA-9} ; bla _{KPC-2} ; oqxA; oqxB; aac(6')-lb-cr; one-step gyrA mutation; parC mutation; aph(3')-la; aadA2; aac(6')-lb; sul1; dfrA12											
28	bla _{SHV-12} ; bla _{TEM-1} ; bla _{OXA-9} ; bla _{KPC-3} ; bla _{SHV-11} ; OmpK35 and OmpK36 truncation; aac(6')-lb-cr; oqxA; oqxB; one-step gyrA mutation; parC mutation; aac(6')-lb; aph(3")-lb; aadA1; sul2; dfrA14; premature stop codon in mgrB											
29	bla _{SHV-1} ; bla _{NDM-1} ; bla _{CTX-M-15} ; bla _{CMY-4} ; OmpK35 truncation; qnrB1; aac(6')-lb- cr; oqxA; oqxB; one-step gyrA mutation; parC mutation; rmtf; aacA4; aph(3')-VIa; aadA2; sul1; dfrA12											
30	bla _{SHV-11} ; bla _{TEM-1} ; bla _{OXA-2} ; bla _{KPC-3} ; OmpK36 truncation; <i>phoP</i> mutation; <i>aac(6')-lb-cr; oqxA</i> ; <i>oqxB</i> ; <i>qnrS1</i> ; two- step <i>gyrA</i> mutation; <i>parC</i> mutation; <i>aadA8b</i> ; <i>aadA1</i> ; <i>aadA2</i> ; <i>aac(3)-lla</i> ; <i>aacA4</i> ; <i>aac(3)-lla</i> ; <i>aacA4</i> ; <i>aph(3')-la</i> ; <i>sul1</i> ; <i>sul3</i> ; <i>dfrA12</i>											
31	bla _{CTX-M-15} ; bla _{TEM-1} ; bla _{SHV-83} ; OmpK36 truncation; oqxA; oqxB; qnrB1; aph(6)- ld; aph(3")-lb; sul2; dfrA14											
32	bla _{OXA-1} ; bla _{SHV-11} ; bla _{CTX-M-15} ; bla _{TEM-1B} ; OmpK36 truncation; oqxA; oqxB; qnrB1; aac(6')-lb-cr; tet(A); aph(6)-ld; aph(3")-lb; sul2; dfrA14											

33	<pre>bla_{LEN-12}; bla_{SHV-1}; OmpK36 truncation; oqxA; oqxB; tet(D); sul2; dfrA14</pre>																						
34	<i>bla</i> _{SHV-71} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>																						
35	<i>bla</i> _{SHV-1} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>																						
36	<pre>bla_{SHV-36}; OmpK36 truncation; oqxA; oqxB; ant(2")-la</pre>																						
37	bla _{TEM-1} ; bla _{KPC-3} ; bla _{SHV-26} ; bla _{SHV-30} ; OmpK36 truncation; ant(2″)-la; qnrS1																						
38	bla _{OKP-B2} ; bla _{TEM-1} ; bla _{SHV-122} ; OmpK36 truncation; oqxA; oqxB; tet(D); sul2; dfrA26																						
39	<i>bla</i> _{SHV-62} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>																						
40	<i>bla</i> _{SHV-83} ; OmpK36 truncation; <i>oqxA</i> ; <i>oqxB</i>																						
	Overall agreement	8	5%	9	5%	9	8%	8	5%	9	- 5%	85	5%	9!	5%	98	3%	98	8%	8	0%	93	%
	212																						
	213																						
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Gene ¹	One copy	Ten copies	Forty copies	Fifty copies	One hundred
	(minutes)	(minutes)	(minutes)	(minutes)	copies
					(minutes)
β-lactam genes					
Non-ESBL TEM enzymes	0.39 minutes	13 minutes	66 minutes	78 minutes	155 minutes
	(IQR 0.14-2)	(IQR 8-16)	(IQR 54-74)	(IQR 71-99)	(IQR 136-174)
Non-ESBL OXA enzymes	0.91 minutes	20 minutes	75 minutes	92 minutes	163 minutes
	(IQR 0.6-4.8)	(IQR 14-22)	(IQR 55-83)	(IQR 66-99)	(IQR 125-177)
Non-ESBL SHV enzymes	0.6 minutes	13 minutes	57 minutes	73 minutes	146 minutes
	(IQR 0.1-1.1)	(IQR 9-17)	(IQR 48-69)	(IQR 60-87)	(IQR 129-170)
ESBL SHV enzymes	1.1 minutes	17 copies	57 minutes	74 minutes	125 minutes
	(IQR 0.03-1.9)	(IQR 12-17)	(IQR 52-63)	(IQR 73-75)	(IQR 106-139)
ESBL CTX-M-type enzymes	0.5 minutes	11 minutes	50 minutes	64 minutes	138 minutes
	(IQR 0.14-1.4)	(IQR 10-14)	(IQR 40-66)	(IQR 46-86)	(IQR 102-164)
ESBL OXA enzymes	0.58 minutes	16 minutes	61 minutes	75 minutes	165 minutes
	(IQR 0.1-1.3)	(IQR 0.1-0.2)	(IQR 55-71)	(IQR 72-90)	(IQR 148-184)
KPC carbapenemases	0.33 minutes	12 minutes	57 minutes	74 minutes	150 minutes
	(IQR 0.1-1.1)	(IQR 7-14)	(IQR 49-71)	(IQR 66-90)	(IQR 131-169)
NDM carbapenemases	0.7 minutes	14 minutes	50 minutes	64 minutes	153 minutes
	(IQR 0.01-0.9)	(IQR 3-26)	(IQR 23-116)	(IQR 35-173)	(IQR 85-489)
Aminoglycoside inactivating enzymes	-			_	
Aminoglycoside modifying enzymes	1.0 minute	15 minutes	66 minutes	82 minutes	151 minutes
	(IQR 0.3-4)	(IQR 9-24)	(IQR 50-80)	(IQR 61-99)	(IQR 130-172)
Ribosomal RNA methyltransferase	0.6 minutes	12 minutes	55 minutes	70 minutes	132 minutes
mutations	(IQR 0.3-0.9)	(IQR 8-15)	(IQR 41-69)	(IQR 58-81)	(IQR 116-148)
Tetracycline resistance genes			-	_	-
tet(A), tet(B), tet(D), tet(G)	0.9 minutes	11 minutes	59 minutes	73 minutes	133 minutes
	(IQR 0.4-1.8)	(IQR 7-18)	(IQR 38-73)	(IQR 54-89)	(IQR 116-166)
Trimethoprim/sulfamethoxazole related gen	nes				
dfrA genes	0.2 minutes	14 minutes	68 minutes	85 minutes	164 minutes
	(IQR 0.02-0.5)	(IQR 7-16)	(IQR 53-75)	(IQR 69-92)	(IQR 136-180)
sul genes	0.5 minutes	13 minutes	57 minutes	80 minutes	166 minutes
	(IQR 0.27-1.3)	(IQR 7-18)	(IQR 45-76)	(IQR 65-96)	(IQR 131-173)

Supplemental Table 4: Average time to detection of resistance genes based on the number of reads detected in minutes

¹Only including genes detected in at least three isolates; ESBL: extended-spectrum beta-lactamase