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An overview and analysis

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Abbreviations

Ag	antigen
AMR	antimicrobial resistance
BCG	Bacillus Calmette–Guérin
BMGF	Bill & Melinda Gates Foundation
CF	colonization factor
CFA	colonization factor antigen
CgoX	coproporphyrinogen oxidase
CHIM	Controlled Human Infection Model
CJCV	capsule conjugate *Campylobacter* vaccine
CMV	cytomegalovirus
COPS	Group D core + O-polysaccharide
COVID-19	coronavirus disease
CP, CPS	capsular polysaccharide
CS	coli surface
dmLT	double-mutant *Escherichia coli* heat-labile toxin
dPNAG	deacylated poly-N-β-(1-6)-acetyl-glucosamine
DT	diphtheria toxoid
EPA	ExoProtein A; a detoxified form of *Pseudomonas aeruginosa* Exotoxin A
ETEC	enterotoxigenic *Escherichia coli*
ExPEC	extraintestinal pathogenic *Escherichia coli*
FTA	fimbrial tip adhesin
GAPDH	glyceraldehyde 3-phosphate dehydrogenase
Gates MRI	Bill & Melinda Gates Medical Research Institute
Gavi	Gavi, the Vaccine Alliance
GGT	gamma-glutamyl transpeptidase
GHIT	Global Health Innovative Technology Fund
GMMA	generalized modules for membrane antigens
GVGH	GSK Vaccine Institute for Global Health
Hib	*Haemophilus influenzae* type B
HICs	high-income countries
HKMS	heat-killed multi-serotype *Shigella* immunogens
HLA	human leucocyte antigen
HtrA	protease high temperature requirement A
IATS	International Antigenic Typing Schema
IAVI	International AIDS Vaccine Initiative
ICMR	Indian Council of Medical Research
ICU	intensive care unit
IDRI	Infectious Disease Research Institute
iNTS	invasive non-typhoidal *Salmonella*
IPD	invasive pneumococcal disease
IVI	International Vaccine Institute
LMICs	low- and middle-income countries
LPS	lipopolysaccharide
LT	*Escherichia coli* heat-labile toxin
MAPS	multiple antigen presenting system
MDR	multidrug-resistant
MEFA	multiepitope fusion antigen
MIP	*Mycobacterium indicus pranii*
MSM	men who have sex with men
Mtb	*Mycobacterium tuberculosis*
MVA	modified Vaccinia virus Ankara
NDA	New Drug Application
NIAID	National Institute of Allergy and Infectious Disease
NICED	National Institute of Cholera and Enteric Diseases
NICHD	National Institute of Child Health and Human Development
NIH	National Institutes of Health
NIHCC	NIH Clinical Center
NMRC	Naval Medical Research Center
NOMVs	native outer membrane vesicles
NRA	national regulatory authority
NTS	non-typhoidal *Salmonella*

OMP	outer membrane protein
OMV	outer membrane vesicle
PBPV	protein-based pneumococcal vaccine
PCV	pneumococcal conjugate vaccine
PDVAC	Product Development for Vaccines Advisory Committee
Pephyd	peptidoglycan hydrolase
PPrV	pneumococcal protein vaccine
PSSP-1	pan-*Shigella* surface protein 1
PPSV	pneumococcal polysaccharide vaccine
R&D	research and development
rBCG	recombinant BCG
rTSST-1v	recombinant toxic shock syndrome toxin-1 variant
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SEB	staphylococcal enterotoxin B
ser.	serovar
spp.	species
SSI	Staten Serum Institute
SsIE	secreted and surface-associated lipoprotein from *Escherichia coli*
ST	*Escherichia coli* heat-stable toxin
TB	tuberculosis
TBVI	TuBerculosis Vaccine Initiative
TCV	typhoid conjugate vaccine
TLR	toll-like receptor
TPI	triose-phosphate isomerase
TPP	target product profile
TPV	typhoid polysaccharide vaccine
TT	tetanus toxoid
UPEC	uropathogenic *Escherichia coli*
US FDA	US Food and Drug Administration
UTI	urinary tract infection
Vi	capsular virulence antigen
ViPS	Vi polysaccharide
virG	*Shigella* outer membrane protein essential for bacterial spreading
WHO	World Health Organization
WHO SAGE	WHO Strategic Advisory Group of Experts on Immunization
WHO BPPL	WHO Bacterial Priority Pathogens List
WRAIR	Walter Reed Army Institute of Research

Executive summary

Vaccines can be highly effective tools in combating antimicrobial resistance (AMR). They reduce the incidence of both resistant and susceptible infections, thereby also decreasing antibiotic consumption. Advances in vaccine technology in recent decades have made developing vaccines against previously challenging targets possible. There is a need to understand what vaccines are currently in development and those which may be available as tools to contribute to controlling AMR in the future. This analysis considers vaccine candidates in preclinical and clinical development against pathogens on the 2017 WHO Bacterial Priority Pathogens List (WHO BPPL), in addition to *Clostridioides difficile* and *Mycobacterium tuberculosis.* Sixty-one vaccine candidates in active clinical development and 94 candidates in confirmed active preclinical development were identified.

The report identified four groups of pathogens with vaccine candidates in various stages of clinical development, and with varying degrees of feasibility for vaccine development.

The first group (Group A) contains pathogens with vaccines already licensed. These exist against four priority pathogens for AMR: *Salmonella enterica* ser. Typhi, *Streptococcus pneumoniae, Haemophilus influenzae* type b (Hib), and *Mycobacterium tuberculosis*. The effectiveness of the vaccine against S. pneumoniae dramatically reduced mortality in the United States of America (USA) and Europe in comparison to other regions where the vaccine is not widely available and used. The coverage of authorized vaccines should be increased to maximise their impact on AMR. Current Bacillus Calmette-Guérin (BCG) vaccines against tuberculosis (TB) do not adequately protect against TB and the development of more effective vaccines against TB should be accelerated.

The second group (Group B) includes pathogens with vaccines that are in late-stage clinical trials with high development feasibility: extraintestinal pathogenic *Escherichia coli* (ExPEC), *Salmonella enterica* ser. Paratyphi A, *Neisseria gonorrhoeae*, and *Clostridioides difficile.* Hence, for two out of the six leading pathogens for deaths associated with AMR (1), a vaccine either already exists, as for *S. pneumoniae,* or maybe feasible, as for *E. coli.* R&D efforts and development of vaccines in late-stage clinical trials should be continued and where possible accelerated.

The third group (Group C) contains pathogens with vaccine candidates either in early clinical trials or with moderate to high feasibility of vaccine development: enterotoxigenic *E. coli* (ETEC), *Klebsiella pneumoniae,* non-typhoidal *Salmonella* (NTS), *Campylobacter* spp., and *Shigella* spp. Vaccines against these pathogens might be available in the long term, however, short term solutions to prevent resistance should focus on other interventions to reduce AMR.

The fourth group (Group D) contains pathogens with a small number or no vaccine candidates in the pipeline and low vaccine development feasibility: *Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter* spp., *Enterococcus faecium, Staphylococcus aureus,* and *Helicobacter pylori*. Vaccines against these pathogens are unlikely to be available in the short term, and alternative interventions to prevent AMR caused by these pathogens should be considered. It is even more worrying that the drug development pipeli-