options mprint mlogic symbolgen mprint symbolgen mlogic nocenter missing=" ";
title;
footnote;
proc datasets library=WORK kill nolist nodetails;
quit;
%let prot=/Volumes/app/cdars/prod/sites/cdars4/prjC459/nda2_unblinded_esub/euaext_esub_adam/saseng/cdisc3_0;
libname datvprot "&prot./data_vai" access=readonly;
%let codename=adc19ef-ve-cov-7pd2-peds-wo-eval;
%let outlog=&prot./analysis/esub/logs/&codename..log;
%let outtable=&prot./analysis/esub/output/&codename..html;
proc printto log="&outlog" new;
run;
/**** Population Flag ****/
proc sql;
create table popf as select distinct usubjid, evaleffl, trt01pn, trt01p, aai2effl
from datvprot.adsl
where EVALEFFL='Y' and MULENRFL ne "Y" and PHASEN ne 1 and HIVFL = 'N' and 12 <= agetr01 <= 15
order by usubjid;
quit;
proc sql;
create table adc19ef as select *
from datvprot.adc19ef
order by usubjid;
quit;
data tpop;
merge adc19ef (in = a) popf (in = b);
by usubjid;
if a*b;
run;
/***** Total Population *****/
proc sql;
create table dsin as select distinct subjid, trt01pn, trt01p, paramn, paramcd, param, CDCRMUFL, CDP27FL,
PDRMUPFL, aval, avalc, evaleffl, PDP27FL, pdrmufl, ILD27FL, filocrfl, usubjid, aai2effl, PDP214FL, ILD214FL, CDRMUPFL, adt, dvstdt
from tpop;
quit;

proc sql noprint;
  select bign into :n1 - :n2
  from (select count(distinct usubjid) as bign, trt01pn
       from dsin
       where PDP27FL = "Y"
       group by trt01pn)
  order by trt01pn;
quit;

%let n1 = &n1.;
%let n2 = &n2.;

%put &n1 &n2.;

/*** Subjects at Risk ****/

proc sql;
  create table riskp as select distinct usubjid, trt01pn, trt01p, aval
  from dsin
  where PDRMUPFL = "N" and PDP27FL = "Y" and paramcd in ("ST27PD") and aval > 0;
quit;

proc sql;
  create table n2 as select count(distinct usubjid) as n2, trt01pn
  from riskp
  group by trt01pn
  order by trt01pn;
quit;

/***** Events (n1) *****/

proc sql;
  create table evnts as select distinct usubjid, param, avalc, trt01pn
  from dsin
  where paramcd in ("C19ONST") and upcase(ILD27FL) = "Y" and upcase(FILOCRRFL) = "Y" and ((not missing(DVSTDT) and adt <= DVSTDT) or missing(DVSTDT))
  and usubjid in (select distinct usubjid from riskp)
  order by usubjid;
quit;

proc sql;
  create table evtn as select count(distinct usubjid) as smln, trt01pn
  from evnts
  group by trt01pn
  order by trt01pn;
quit;

/**** Make sure All treatment arms are present in EVTN dataset (with 0 cases) *****/
from dsin
order by trt01pn;
quit;

data evtn;
merge evtn (in=a) trt_u (in=b);
by trt01pn;
if b;
if missing(smln) then smln = 0;
run;

/*** Surveillance Time ****/

proc sql;
create table st as select distinct usubjid, aval, trt01pn, trt01p, paramcd
from dsin
where paramcd in ("ST27PD") and
usubjid in (select distinct usubjid from riskp);
quit;

proc sql;
create table riskn as select a.*, b.ptyrs, pty
from  n2 a inner join
(select (sum(aval)/365.25/1000) as ptyrs, sum(aval)/365.25 as pty, trt01pn
from st group by trt01pn) b on a.trt01pn = b.trt01pn;
quit;

proc sql;
create table pt as select strip(put(a.smln,best.)) as evtn, b.*, smln/ptyrs as ir,
a.smln, (put(ptyrs, 7.3) || "(" || strip(put(n2,best.))) || ")" as ptyb
from evtn a inner join
riskn b on a.trt01pn = b.trt01pn;
quit;

/*** Total cases ****/
proc sql noprint;
select sum(smln) into :ncases
from pt;
quit;

%let ncases = &ncases.;

/*** Cases in Vacination Group ****/
proc sql noprint;
select smln into :nv1:-nv2 from pt;
quit;

%let nv1 = &nv1;
%let nv2 = &nv2;
%let ncases = &ncases;
%let ve = 0.3;
%put No. of Cases in Vacination group are &nv1.;
%put Total No. of Cases in the trial are &ncases.;

proc transpose data = pt out = tr prefix = trt;
  var ptyrs;
  id trt01pn;
run;

data tr;
  set tr;
  *IRR=trt8/trt9;
  n_p = &ncases - &nv1.;
  r = trt8/trt9;
  P = R*(1-&VE)/(1+R*(1-&VE));
  IR_V=&nv1/trt8;
  IR_P=n_p/trt9;
  alpha = 0.05;
  length VE lcl ucl $25.;
  VE=strip(put(100*(1-IR_V/IR_P),7.1));
  pr = put(CDF('BETA',p,0.700102+&nv1,1+&ncases-&nv1),7.4);
  pr_n = CDF('BETA',p,0.700102+&nv1,1+&ncases-&nv1);
  qh_theta = quantile('BETA',0.975,0.700102+&nv1,1+&ncases-&nv1);
  ql_theta = quantile('BETA',0.025,0.700102+&nv1,1+&ncases-&nv1);
  QH = round (100*(R - qL_theta*(R+1))/(R*(1-qL_theta)), 0.01);
  QL = round (100*(R - qH_theta*(R+1))/(R*(1-qH_theta)), 0.01);

*** Use Clopper-Pearson Method to display CI ****;
  fu = finv( 1- alpha/2, 2*(&nv1.+1), 2*N_P);
  ucl_pi = (&nv1.+1)*fu/(N_P + (&nv1.+1)*fu);
  fl = finv(1-alpha/2, 2*(N_P+1), 2*&nv1.);
  if &nv1 = 0 then lcl_pi = 0;
  else lcl_pi = &nv1./(&nv1. + fl*(N_P+1));
  ucl_theta = ucl_pi/(r*(1-ucl_pi));
  lcl_theta = lcl_pi/(r*(1-lcl_pi));
  qu = 100*(1 -lcl_theta);
  ql = 100*(1 - ucl_theta);
  if not missing(ql) then lcl = strip(put(ql,8.1));
  if not missing(qu) then ucl = strip(put(qu,8.1));
  else ucl = 'NE';
  vci = "(" || strip(lcl) || ", " || strip(ucl) || ");

**** END ****;

text = "First COVID-19 occurrence from 7 days after Dose 2";
  /**** If probablity is 0 then show <0.0001' and if its 1 then then show >0.9999 *****/
  if pr_n < 0.0001 then pr = '<0.0001';
  else if pr_n > 0.9999 then pr = '>0.9999';
  /**** If VE is missing then show infinity symbol ****/
  if strip(ve) = '.' then do; ve = "-(*ESC*){unicode 221e}"; vci = "(NA, NA)"; end;
run;

proc transpose data = pt out = trn prefix = trtn;
  var evtn;
  id trt01pn;
run;
proc transpose data = pt out = try prefix = trty;
  var ptyb;
  id trt01pn;
run;
proc sql;
  create table final as select a.*, b.*, c.*
    from trn (drop = _name_) a,
        try (drop = _name_) b,
        tr (drop = _name_) c;
quit;

****** Set up Report ******;
ods escapechar="~";
ods html file="~outtable."

title1 "Vaccine Efficacy (*ESC*){unicode 2013} First COVID-19 Occurrence From 7 Days After Dose 2";
title2 "(*ESC*){unicode 2013} Blinded Placebo-Controlled Follow-up Period";
title3 "(*ESC*){unicode 2013} Subjects 12 Through 15 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2";
title4 "(*ESC*){unicode 2013} Evaluable Efficacy (7 Days) Population";
footnote1 "Abbreviations: N-binding = SARS-CoV-2 nucleoprotein(*ESC*){unicode 2013}binding; NAAT = nucleic acid amplification test; ~nSARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.";
footnote2 "Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.";
footnote3 "a.(*ESC*){nbspace 5}N = number of subjects in the specified group. ~nb.(*ESC*){nbspace 5}n1 = Number of subjects meeting the endpoint definition.";
footnote4 "c.(*ESC*){nbspace 5}Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.";
footnote5 "d.(*ESC*){nbspace 5}n2 = Number of subjects at risk for the endpoint.";
footnote6 "e.(*ESC*){nbspace 5}Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.";

proc report data = final nowd headline headskip split = "*" style(report)=[];
column (text ("Vaccine Group (as Randomized)~{line}" ("BNT162b2 (30 ~{unicode 03BC}g)*(N~{super a}=&n1.)" trtn8 trty8) ("Placebo*(N~{super a}=&n2.)" trtn9 trty9)) ve vci);
define text / "Efficacy Endpoint" flow style(header)=[just=l] style(column)=[cellwidth=3in just=l];
define trtn8 / " n1~{super b}" style(column)=[cellwidth=0.8in just=c];
define trty8 / "Surveillance*Time~{super c} (n2~{super d})" style(column)=[cellwidth=1.5in just=c];
define trtn9 / " n1~{super b}" style(column)=[cellwidth=0.8in just=c];
define trty9 / "Surveillance*Time~{super c} (n2~{super d})" style(column)=[cellwidth=1.5in just=c];
define ve / " VE (%)" style(column)=[cellwidth=0.5in just=c];
define vci / " (95% CI~{super e})" style(column)=[cellwidth=0.5in just=c];
run;
ods HTML close;
proc printto;
run;