# Consideration of Effective Seroprotection Rate (eSPR) and Cost Per Protected Patient (CPP) as Estimates of Real-World Outcomes in Adult Hepatitis B Virus (HBV) Vaccination

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## Background

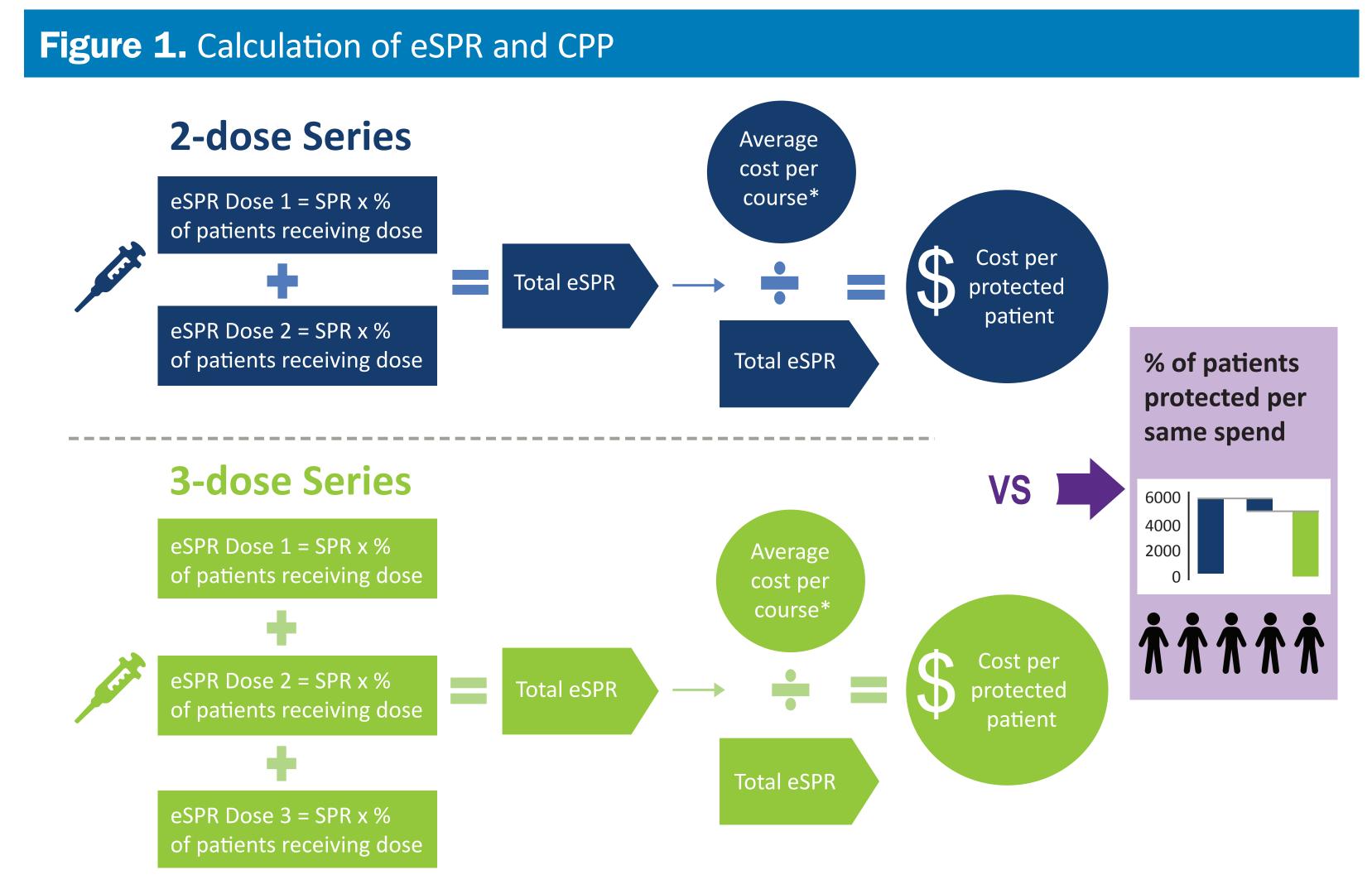
- HBV infection is associated with considerable public health burden due to prevalence, healthcare costs, and lack of curative therapies
- The CDC Advisory Committee on Immunization Practices (ACIP) recommends preventative vaccination for adults at risk of HBV infection<sup>1</sup>
- Currently available adult HBV vaccines include 2- and 3-dose series
- Legacy 3-dose HBV vaccines (ENGERIX-B<sup>®</sup>, Hepatitis B Vaccine [Recombinant], GlaxoSmithKline<sup>®</sup>; RECOMBIVAX HB<sup>®</sup>, Hepatitis B Vaccine [Recombinant], Merck) are labeled for administration on a 0-, 1-, and 6-month schedule<sup>2,3</sup>
- The 2-dose HBV vaccine (HEPLISAV-B<sup>®</sup>, Hepatitis B Vaccine [Recombinant], Adjuvanted, Dynavax Technologies Corporation) is administered with a 4-week dose interval that allows series completion in a single month<sup>4</sup>
- Effectiveness of HBV vaccines in reducing risk of infection is impacted by compliance (ie, series completion according to dosing schedules) and seroprotection rate (SPR) achieved
- Compliance remains suboptimal, particularly for 3-dose vaccines; limited 3-dose series completion rates (as low as 22% to 54%) have been observed in several real-world studies<sup>5-9</sup>
- Poor compliance rates may limit the effectiveness of 3-dose series
- Effectiveness of HBV vaccines is also influenced by patient characteristics; SPR with a full series of a 3-dose vaccine is reduced in certain at-risk populations (eg, people with diabetes mellitus aged <60 years and people with diabetes mellitus aged ≥60 years at the discretion of the treating clinician<sup>10</sup> and some public health populations<sup>5</sup>), as identified by the 2018 ACIP Guidance on HBV vaccination<sup>11</sup>
- The effective SPR (eSPR) is a measure of potential real-world effectiveness that accounts for compliance with dosing regimens. Combined with vaccine costs, eSPR can be used to calculate a cost-per-protected-patient (CPP) measure of cost-effectiveness to determine potential real-world value of a vaccine

# Objective

To determine eSPR and CPP for a 2-dose vs a 3-dose adult HBV vaccine series as measures of real-world clinical- and cost-effectiveness in the general population, a diabetes subpopulation, and a public health subpopulation

## Methods

- This analysis evaluated the 2-dose vaccine HEPLISAV-B<sup>®</sup> and the 3-dose vaccine ENGERIX-B<sup>®</sup>; all adults indicated for administration of HBV vaccination and all sites of care where adult HBV vaccination is administered were included. Public health settings included CDC awardees in local health departments, federally qualified health centers, correctional facilities, STD clinics, and drug treatment facilities<sup>5</sup>
- The model used for calculating eSPR and CPP is shown in Figure 1
- eSPR was calculated using:
- Head-to-head SPR data from Phase 3 registration trials of the 2-dose HBV vaccine administered over 1 month and the 3-dose HBV vaccine administered over 6 months
- Real-world adherence data for the 2-dose and 3-dose vaccine series (by dose)
- CPP was calculated as average cost (cost per dose × percentage of patients receiving that number of doses across the total regimen) ÷ total eSPR, using publicly available vaccine prices<sup>12-14</sup>
- The model applies direct vaccine costs only. It does not include administration cost, which the Centers for Medicare & Medicaid Services attributes as an additional \$20 per dose<sup>15</sup>



CPP=cost per protected patient; eSPR=effective seroprotection rate; SPR=seroprotection rate. \*Average cost for the regimen reflects the sum of the weighted cost per dose. Weighted cost reflects cost per dose × percentage of patients receiving that dose.

## Results

Higher eSPR and lower CPP were evident with the 2-dose vs the 3-dose vaccine in the general population (Table 1), the diabetes subpopulation (Table 2), and the public health subpopulation (Table 3)

Vaccine		Weighted				
(Cost/Dose*)	Dose	Cost, \$ <sup>†</sup>	SPR, %	Patients, % <sup>‡</sup>	eSPR, %	CPP, \$°
2-dose series (\$115.75 per dose)	1	115.75	22.0	40.9	9.0	_
	2	68.41	95.7	59.1	56.6	-
Total		184.16**			65.6	280.91
3-dose series (\$61.86 per dose)	1	61.86	4.2	40.9	1.7	-
	2	36.56	24.0	32.9	7.9	_
	3	16.21	79.5	26.2	20.8	_
Total		114.63**			30.4	376.53

#### Total savings with 2-dose series

CPP=cost per protected patient; eSPR=effective seroprotection rate; SPR=seroprotection rate.

\*Cost/Dose reflects wholesale acquisition cost<sup>12</sup> + federal excise tax. <sup>†</sup>Weighted cost reflects cost/dose × percentage of patients receiving that dose. For dose 2 of a 3-dose regimen, the sum of the percentage of people receiving only 2 doses total + the percentage of people receiving 3 doses total; in this case: 32.9 + 26.2 = 59.1.

<sup>†</sup>Percentage of patients who received a maximum of the number of doses indicated.<sup>16</sup> <sup>°</sup>CPP was calculated as average cost (cost per dose × percentage of patients receiving that number of doses across the total regimen) ÷ total eSPR.

\*\*The average cost for the regimen reflects the sum of the weighted cost per dose for the regimen.

Vaccine (Cost/Dose*)	Dose	Weighted Cost, \$ <sup>+</sup>	SPR, %	Patients, % <sup>‡</sup>	eSPR, %	CPP, \$°
		• •			•	
2-dose series (\$115.75 per dose)	1	115.75	15.4	40.9	6.3	-
	2	68.41	88.9	59.1	52.5	-
Total		184.16**			58.8	312.99
3-dose series (\$61.86 per dose)	1	61.86	2.2	40.9	0.9	-
	2	36.56	6.8	32.9	2.2	-
	3	16.21	65.2	26.2	17.1	-
Total		114.63**			20.2	566.91
Total savings with 2-dose series						253.92

CPP=cost per protected patient; eSPR=effective seroprotection rate; SPR=seroprotection rate.

\*Cost/Dose reflects wholesale acquisition cost<sup>13</sup> + federal excise tax.

<sup>+</sup>Weighted cost reflects cost/dose × percentage of patients receiving that dose. For dose 2 of a 3-dose regimen, the sum of the percentage of people receiving 3 doses total; in this case: 32.9 + 26.2 = 59.1.

\*Percentage of patients who received a maximum of the number of doses indicated.<sup>16</sup>
 \*CPP was calculated as average cost (cost per dose × percentage of patients receiving that number of doses across the total regimen)
 ÷ total eSPR.

\*\*The average cost for the regimen reflects the sum of the weighted cost per dose for the regimen.

#### Table 3. eSPR and CPP in the Public Health Subpopulation\*

Vaccine (Cost/Dose*)	Dose	Weighted Cost, \$ <sup>+</sup>	SPR, %	Patients, %°	eSPR, %	CPP, \$**
2-dose series (\$69.75 per dose)	1	69.75	22.0	59.6	13.1	-
	2	28.18	95.7	40.4	38.7	-
Total		<i>97.93</i> §			51.8	189.14
3-dose series (\$33.52 per dose)	1	33.52	4.2	59.6	2.5	-
	2	13.54	24.0	18.1	4.3	-
	3	7.47	79.5	22.3	17.7	-
Total		54.54 <sup>§</sup>			24.6	221.91

#### Total savings with 2-dose series

CPP=cost per protected patient; eSPR=effective seroprotection rate; SPR=seroprotection rate.

\*The public health subpopulation included HBV vaccinations at CDC awardees in local health departments, federally qualified health centers, correctional facilities, STD clinics, and drug treatment facilities. <sup>+</sup>Cost/Dose reflects wholesale acquisition cost<sup>14</sup> + federal excise tax.

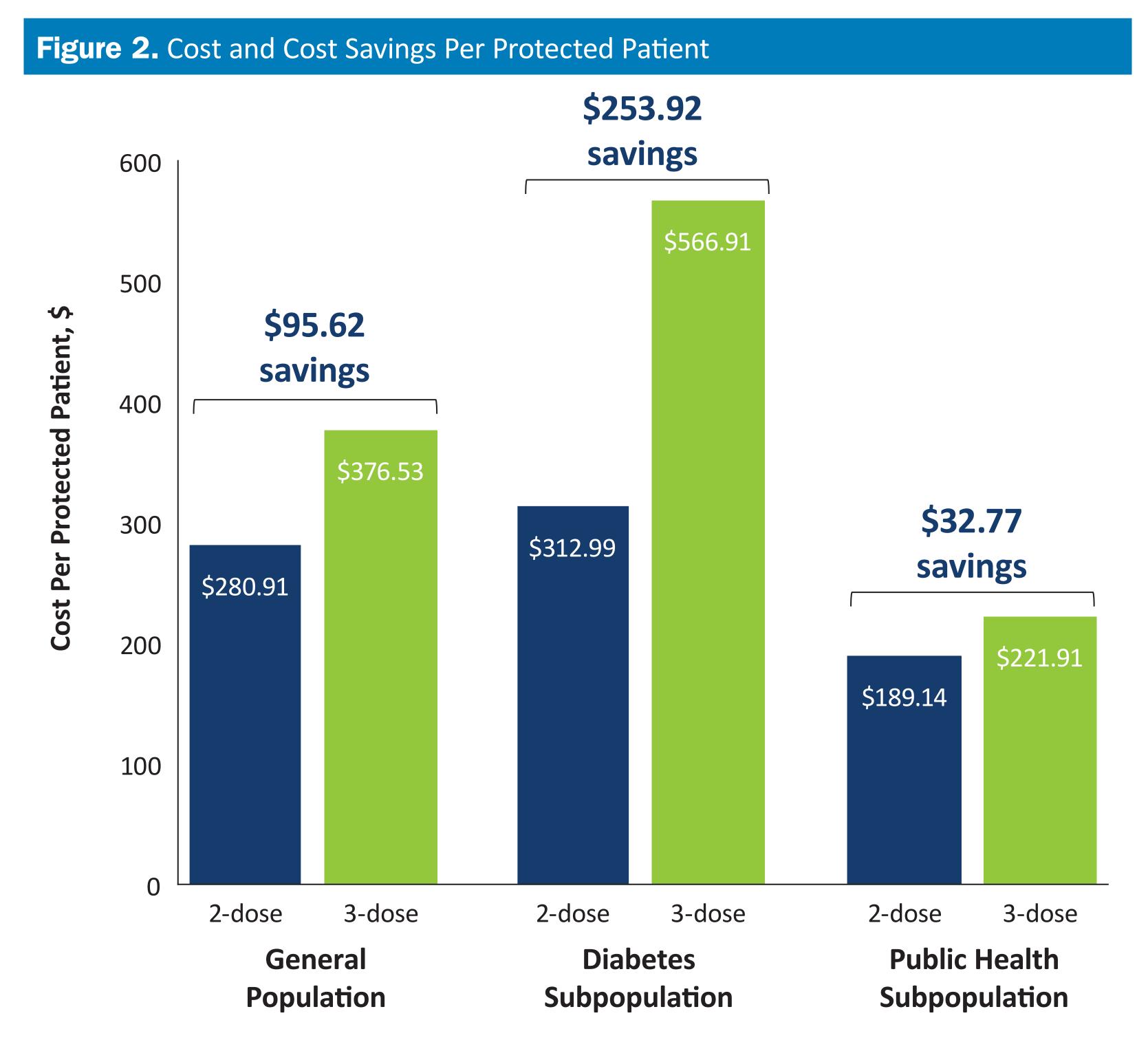
<sup>\*</sup>Weighted cost reflects cost/dose × percentage of patients receiving that dose. For dose 2 of a 3-dose regimen, the sum of the percentage of people receiving 3 doses total; in this case: 18.1 + 22.3 = 40.4. <sup>o</sup>Percentage of patients who received a maximum of the number of doses indicated.<sup>5</sup>

\*\*CPP was calculated as average cost (cost per dose × percentage of patients receiving that number of doses across the total regimen) ÷ total eSPR.

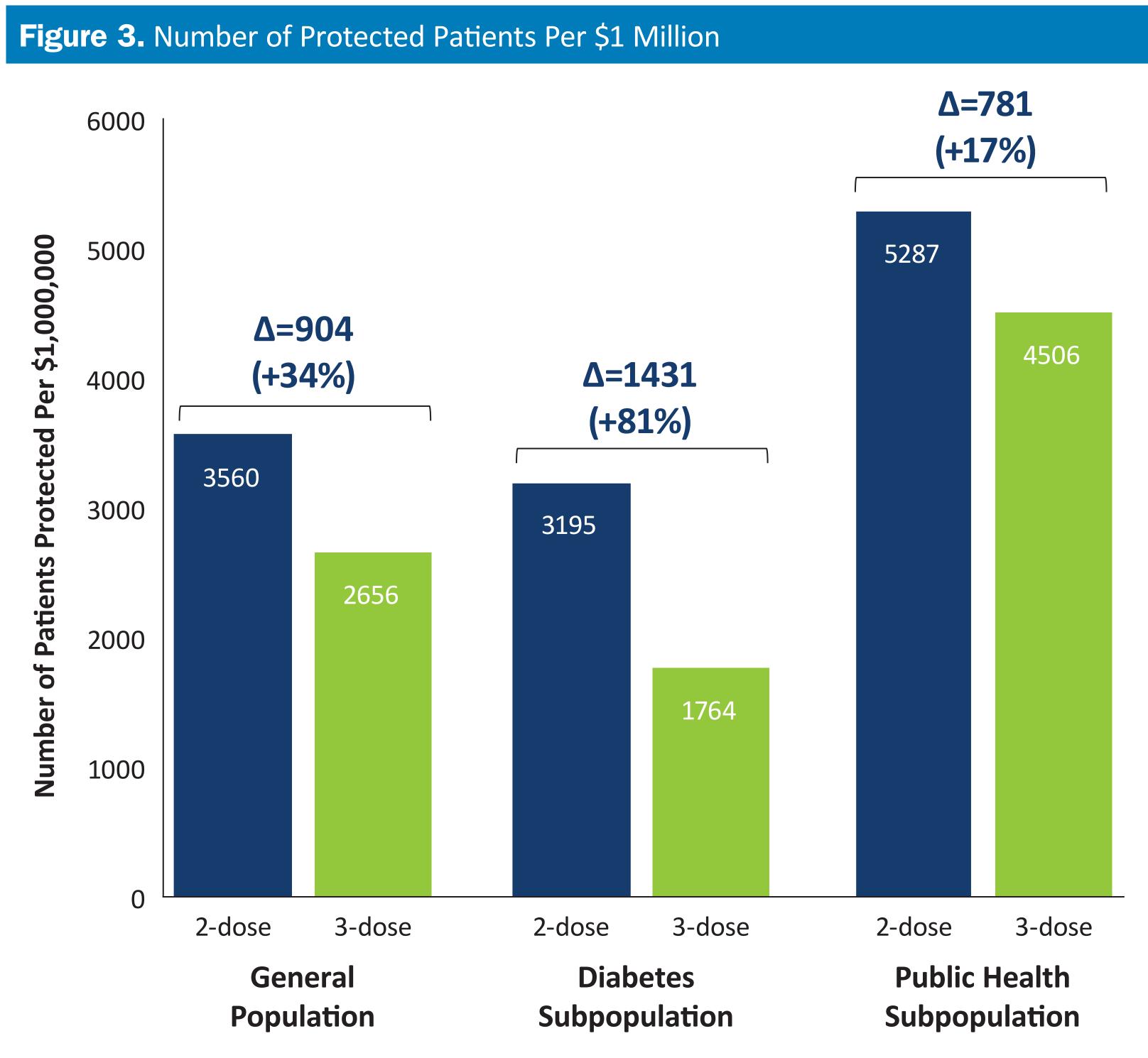
<sup>§</sup>The average cost for the regimen reflects the sum of the weighted cost per dose for the regimen.

32.77

- eSPR achieved with series completion with the 2-dose vs the 3-dose vaccine was approximately
   2-fold greater in the general population (66% vs 30%), 3-fold greater in the diabetes subpopulation (59% vs 20%), and 2-fold greater in the public health subpopulation (52% vs 25%)
- Higher eSPR with the 2-dose vaccine was likely attributable to higher rates of series completion and seroprotection compared with the 3-dose vaccine
- CPP with the 2-dose vs the 3-dose vaccine was \$95.62 less in the general population, \$253.92 less in the diabetes subpopulation, and \$32.77 less in the public health subpopulation (Figure 2)
   The between-vaccine difference in CPP was greater in the diabetes subpopulation (45%) compared with the general population (25%) and the public health subpopulation (15%); this was due in part to the reduced seroprotection conferred by the 3-dose vaccine in people with diabetes



• With equal vaccination spending, 34% more patients in the general population, 81% more patients in the diabetes subpopulation, and 17% more patients in the public health subpopulation can potentially be protected from HBV infection with the 2-dose vs 3-dose vaccine series (Figure 3)



Incremental number and percentage of patients protected with 2-dose vs 3-dose vaccine are indicated above bars.

- To maintain conservative CPP limited to vaccine spend only, administration costs were not included in this analysis. With a \$20 administration cost included<sup>15</sup>, savings associated with the 2-dose series are greater than detailed here:
- General population: \$168.81; incremental patients protected = 51% (vs 34% without administration costs)
- Diabetes subpopulation: \$383.13; incremental patients protected = 104% (vs 81% without administration costs)
- Public health subpopulation: \$110.94; incremental patients protected = 46% (vs 17% without administration costs)

## Conclusions

- eSPR and CPP represent important real-world, valuedriven metrics for comparing clinical- and costeffectiveness of adult HBV vaccines
- In this analysis, a 2-dose HBV vaccine demonstrated higher eSPR and lower CPP compared with a commonly used 3-dose vaccine in both the general population, and in diabetes and public health subpopulations, indicating a potential for greater real-world value and potential cost savings on a CPP basis with the 2-dose series
- This analysis demonstrated that a greater number of patients can be protected from HBV with the 2-dose vaccine than the 3-dose vaccine based on a fixed spend
- Routine evaluation of series completion rates at all care sites that administer adult HBV vaccines is recommended to provide understanding of eSPR and CPP in their institution and to support informed, value-oriented decision making in vaccine selection

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