

Hepatitis B Vaccination Program at Two Tertiary Hemodialysis Centres


WYNNIE LAU, B.SC.(PHARM), PHARM.D., ACPR

KAREN SHALANSKY B.SC.(PHARM), PHARM.D., ACPR, FCSHP

LINDSAY KUFTA, B.SC.(PHARM), PHARMACY RESIDENT

JACEK JASTRZEBSKI, M.D., FRCP(C)

MERCEDI KIAII, M.D., FRCP (C)



Objectives

- Understand hepatitis B markers
 - Hep B surface antigen, Hep B surface antibody, Hep B core antibody
- Review hepatitis B vaccine schedules for dialysis patients
 - Recombivax-HB, Engerix-B
- Discuss Hepatitis B study at 2 major teaching hospitals in Vancouver
 - Response rate to vaccination
 - Factor(s) associated with poor response

Background

Hemodialysis (HD) patients are at an increased risk of hepatitis B infection

- Potential exposure due to improper disinfection of fomites
 - Chair/bed, blood splashes on clothes/gloves, dialysis machine, chart table
- Frequent diagnostic and therapeutic procedures
- Immune dysfunction
- Reduced rates of vaccination response
- Blood transfusions (rare)

All patients have baseline bloodwork drawn upon initiation of dialysis

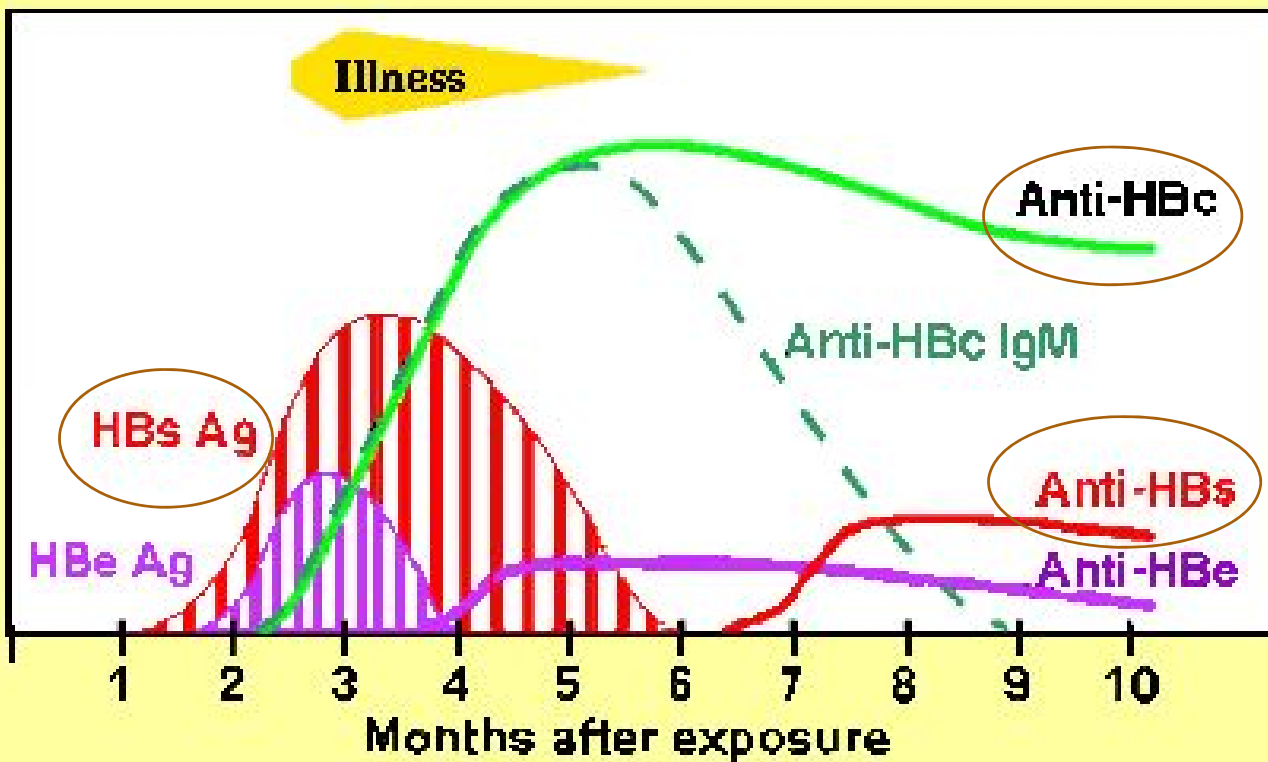
- Vaccination with Hepatitis B vaccine if hepatitis B surface antibody (Anti-HBs) neg

Vaccine Schedule

Vaccine	Normal Adult	Hemodialysis
Recombivax-HB	10 mcg IM at 0, 1, 6 mos	40 mcg IM at 0, 1, 6 mos -Repeat series if Anti-HBs < 10 at month 7
Engerix-B	20 mcg IM at 0, 1, 6 mos	40 mcg IM at 0, 1, 2, 6 mos -Repeat series if Anti-HBs < 10 at month 7
Efficacy (Anti-HBs >10)	95-100% (persists for life)	55-88%

(ASAIO J 1995;41:M717-M719; J Infec Dis 1988;157(2):332-7; Vaccine 1994;12:223-28; Int J Gen Med. 2014;7:109–114.)

Acute Hepatitis Infection



Initial Testing

HBsAg – Hepatitis B surface antigen

- Protein on surface of virus
- Appears 1-10 weeks after acute exposure; undetectable after 4-6 months
- Positive test indicates active infection OR chronic HBV infection

Anti-HBs –Hepatitis B surface antibody

- Appears after disappearance of HBsAg (~6.5-7 months after acute exposure)
- Positive test indicates recovery from active infection OR response to vaccination

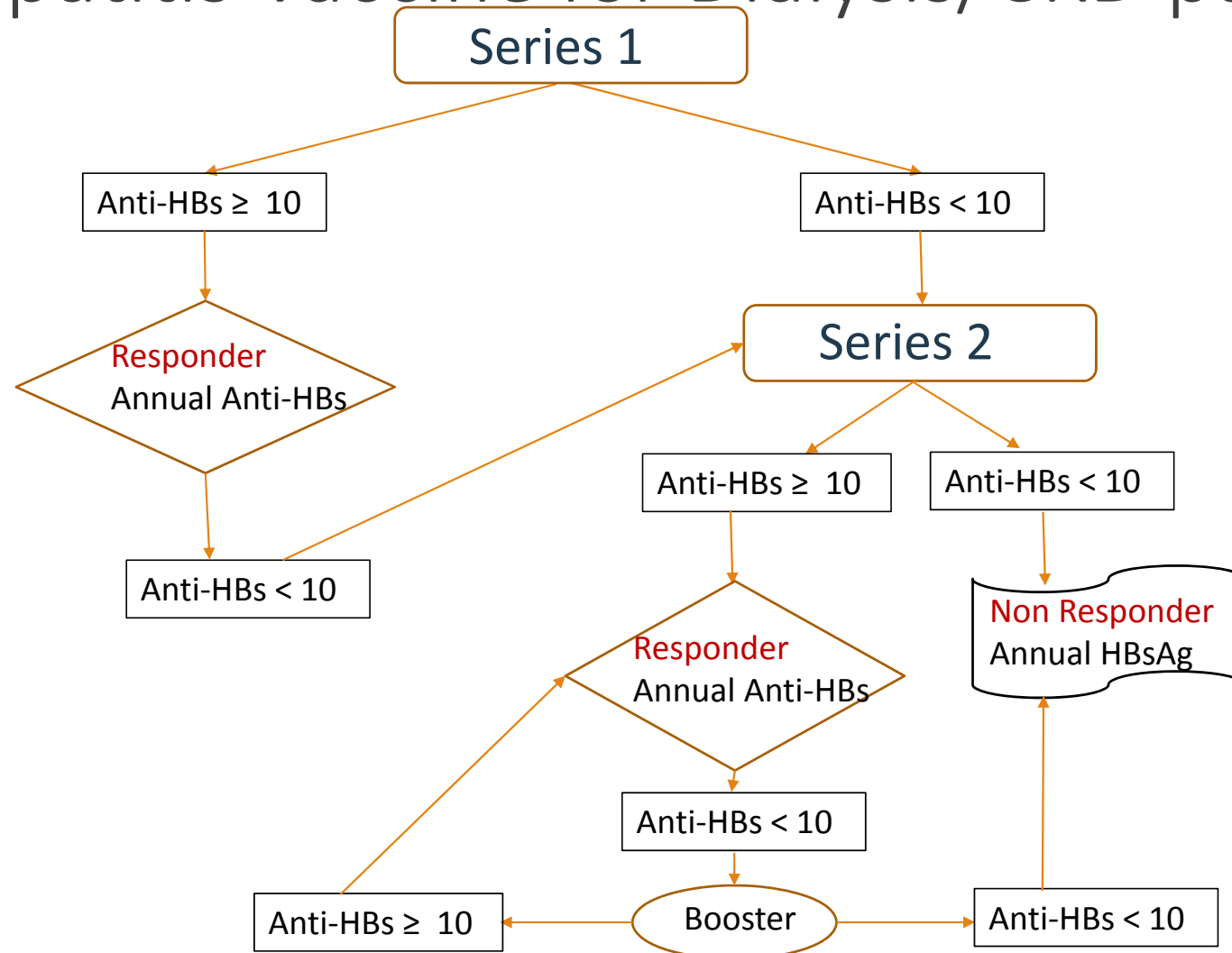
Anti-HBc –Hepatitis B core antibody

- Hepatitis B core is an intracellular antigen expressed in infected hepatocytes (NOT detected in serum; only Anti-HBc detected in serum)
- Appears ~ 2 months after acute exposure (IgM), persists for life (IgG)
- Positive test indicates previous or ongoing infection OR chronic infection OR false (+)

Baseline Scenarios

1. HBsAg positive (irrespective of other values) = **No vaccine**
 - Acutely or chronically infected
2. Anti-HBs ≥ 10 (irrespective of other values) = **No vaccine**
 - Acceptable level of immunity
3. Anti-HBs < 10 ; HBsAg (-); Anti-HBc (-) = **Vaccination**
4. Anti-HBs < 10 ; HBsAg (-); Anti-HBc (+) = **Vaccination** (if HBV DNA < 20)
 - Active infection in window where HBsAg (-), but Anti-HBs not developed yet
 - False positive result (recheck in 1 month)
 - “low level” chronic infection

Hepatitis Vaccine for Dialysis/CKD patients



Vaccination in Dialysis Patients

- Despite a more intense vaccination regimen, vaccination response rates in HD patients are still low
- There may be patient specific factors that affect the response rates
 - e.g. age, comorbidity, immunosuppression, increased BMI, ethnicity

Objectives

Primary Objectives:

- Capture the response rate to Hepatitis B vaccination in HD patients following vaccination series 1, 2, and the booster
- Examine factors associated with responders vs non-responders to hepatitis vaccine
 - NON-RESPONDER = anti-HBs < 10 after receiving series # 2 OR booster

Objectives

Secondary Objectives:

- Evaluate vaccine uptake
 - patient consent/refusal of vaccine
- Examine factors associated with responders vs non-response to hepatitis vaccine after receiving series # 1, 2 or booster
- Determine adherence to vaccination protocol and bloodwork f/u
 - Vaccine # 2: given 4-6 weeks post vaccine # 1
 - Vaccine # 3: given 4.5-5.5 months post vaccine # 2
 - Anti-HBs follow-up: drawn 1-2 months post vaccine # 3 or after booster

Methods

- Retrospective chart review
 - PROMIS database

Inclusion:

- all HD patients since implementation of the new Hepatitis B provincial protocol <http://www.bcrenalagency.ca/resource-gallery/Documents/Hepatitis%20B%20Guideline.pdf>
 - St. Paul's Hospital: Dec 2015-July 2017
 - Vancouver General Hospital: Feb 2016-July 2017

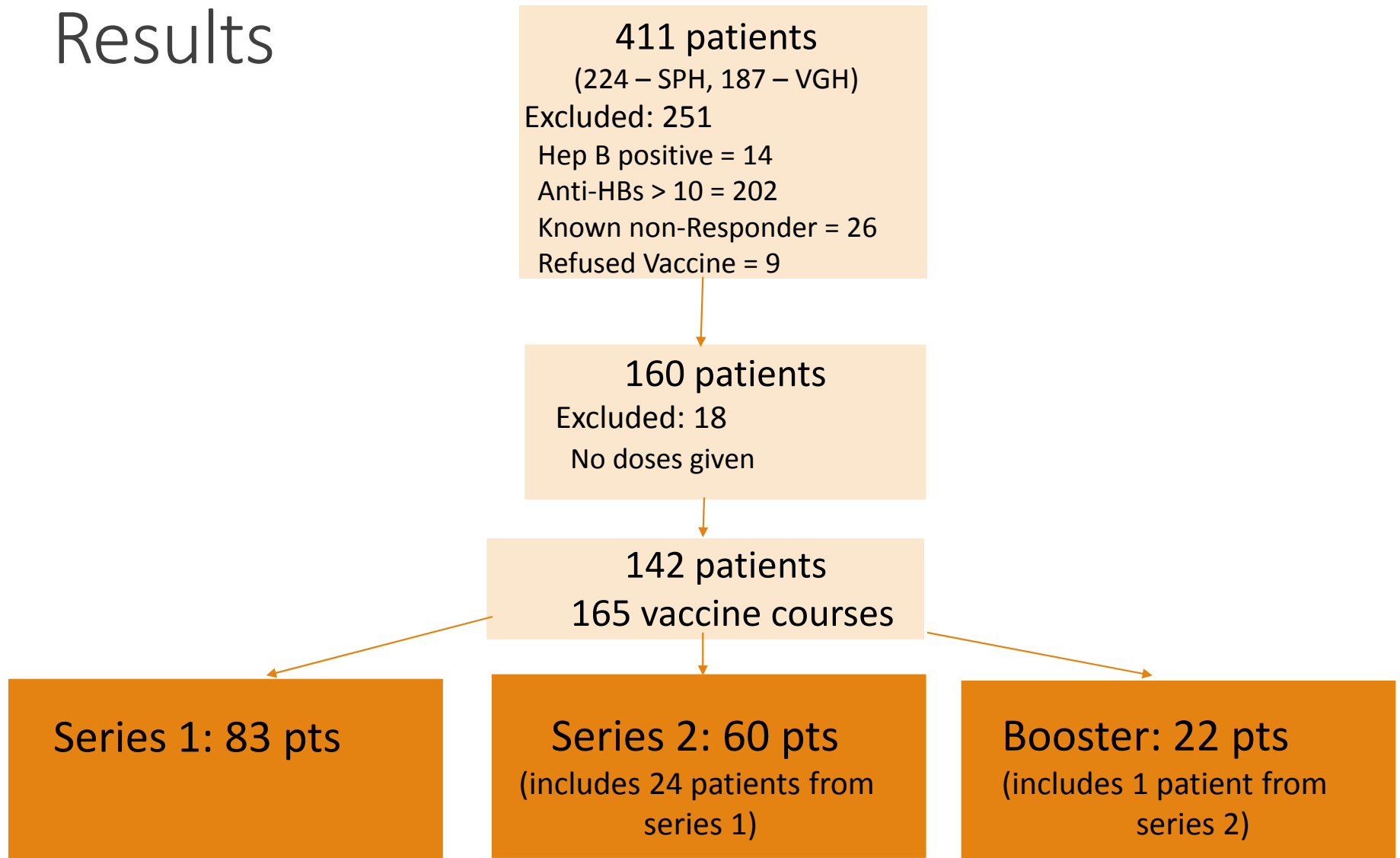
Exclusion:

- Patients not requiring Hepatitis B vaccine
 - Hepatitis B positive patients
 - Anti-HBs > 10 mIU/mL
 - Known non-responders prior to study initiation
 - Patient refusal to receive vaccine

Data Analysis

- Categorical Variables (eg. response rates): **Frequency (%)**
- Quantitative Variables (eg. age, dialysis vintage): **Mean (SD)**
- Comparison between vaccine responders and non-responders:
 - **Univariate analysis** = t-test (Quantitative variables) or Fisher's exact (Categorical variables)
 - **Multivariate logistical analysis**
 - Factors associated with Response Rate

Results



Results – Table 1. Patient Demographics

Variable		N= 142
Hospital, n (%)	SPH	82 (57.7%)
	VGH	60 (42.3%)
Age, mean (SD)		68.9 (13.9)
Gender, Male, n (%)		92 (64.8%)
Ethnicity, n (%)	Caucasian	49 (34.5%)
	Oriental	47 (33.1%)
	Asian Indian	19 (13.4%)
	Filipino	12 (8.4%)
Co-morbidity, n (%)	Diabetes	88 (62%)
	Cancer	23 (16.2%)
	Immunosuppressive Therapy	14 (9.9%)
	Previous Transplant	9 (6.3%)
	Hepatitis C virus	6 (5.3%)
URR, mean (SD)		77.8 (0.31)
Anti-HBc Positive, n (%)		32 (22.5%)
Vaccine Response (Anti-HBs \geq 10), n (%)		
	Series 1 (n=83)	51 (61.4%)
	Series 2 (n=60)	35 (58.3%)
	Booster (n=22)	18 (81.8%)

Primary Outcome: Univariate Analysis (Series 2/booster)

Variable		No Response (N= 29)	Response (N=52)	P-value
Hospital, n (%)	SPH	14 (48.3%)	35 (67.3%)	0.096
	VGH	15 (51.7%)	17 (32.7%)	
Age, mean (SD)		68.4 (13.4)	71.8 (13)	0.267
Gender, Male, n (%)		18 (62.1%)	37 (71.2%)	0.402
Ethnicity, n (%)	Caucasian	18 (62.1%)	16 (30.8%)	0.253
	Oriental	5 (17.2%)	19 (36.5%)	0.668
	Asian Indian	2 (6.9%)	7 (13.5%)	0.772
	Filipino	2 (6.9%)	5 (9.6%)	0.270
Co-morbidity, n (%)	Diabetes	16 (55.2%)	36 (69.2%)	0.208
	Cancer	7 (24.1%)	9 (17.3%)	0.461
	Immunosuppressive Therapy	4 (13.8%)	3 (5.8%)	0.231
	Previous Transplant	2 (6.9%)	2 (3.8%)	0.549
	Hepatitis C virus	3 (10.3%)	1 (1.92%)	0.133
URR, mean (SD)		78.4 (5.8)	78.3 (6.1)	0.930
Anti-HBc Positive, n (%)		4 (13.8%)	12 (23.1%)	0.319
Adherence to Protocol, Yes, n (%)		9 (31%)	29 (55.8%)	0.035

Multivariate Analysis

Primary Outcome N=81 (Series 2 + booster)

Estimated odds of response for adherent regimen:

- 2.41 (95% CI: 0.89-6.80, $p=0.08$)

Secondary Outcome N=140 (Series 1, 2 + booster)

(overlapping pts excluded ie. 25 non-responders from series 1 who received series 2)

Estimated odds of response for adherent regimen:

- 2.2 (95% CI: 1.41-3.44, $p=0.0005$)

Adherence

Vaccination Series	Site A	Site B
Series 1	N= 39	N=47
vaccine 1 → 2 (4-6 weeks post)	82%	91%
vaccine 2 → 3 (4.5-5.5 mos post)	54%	81%
vaccine 3 → BW (1-2 mos post)	59%	57%
missed doses (1 or 2)	13% (N=5)	6% (N=3)
Series 2	N=26	N=34
vaccine 1 → 2 (4-6 weeks post)	73%	68%
vaccine 2 → 3 (4.5-5.5 mos post)	88%	65%
vaccine 3 → BW (1-2 mos post)	50%	74%
missed doses (1 or 2)	8% (N=2)	9% (N=3)
Booster	N=7	N=15
vaccine → BW (1-2 mos post)	29%	80%
Positive Response if Adherent	1.39 x more likely to respond	1.32 x more likely to respond

Discussion

- Vaccine response rate for HD patients similar to literature
 - 61% series 1; 58% series 2
- **Adherence** important factor in determining response
 - More frequent assessment by nursing of hepatitis status (biannually)
 - Double checks by nephrologist/nurse educator/pharmacist
 - Site A – review hepatitis assessment forms Q3months with (small) BW monitoring
 - Site B - pharmacist regularly monitors Hepatitis B bloodwork
 - Improve documentation of when to draw Anti-HBs levels post-vaccine
 - Annual nursing in-services on Hepatitis B
 - stressing importance of adherence to regimen

Discussion

(Int J Gen Med 2014;7:109-113)

N= 83 HD patients receiving Engerix-B 40 mcg at months 0, 1, 2, 6

- Responders = 49 (59%)
 - Poor Responders (Anti-HBs 10-100) = 18 (22%)
 - Good Responders (Anti-HBs > 100) = 31 (37%)
- Factors influencing response (Univariate analysis):
 - **Diabetes** (p=0.02) and **Hypertension** (p=0.01)
 - Other Studies: age > 60, concomitant HCV or HIV, diabetes, low dialysis adequacy
(Clin Nephrol 2002;58:301-4; J Natl Med Assoc 2006;98:1953-7; Am J Nephrol 1996;16:95-7)
- Trend to reduction in Antibody titres at 1 year f/u
 - 55% Poor Responders had Anti-HBs titres fall to < 10
 - 0% of Good Responders had Anti-HBs titres fall to < 10

Limitations

- Small numbers
 - Limited number of subgroups (e.g. ethnicity, co-morbidities, HCV status)
- Retrospective design
 - Possibility that not all vaccine doses documented in chart or in PROMIS
 - Difficult to differentiate past vs present conditions e.g. cancer, HCV
 - Difficult to assess if missed/late doses due to acute hospital admission

Conclusion

- Understand hepatitis B markers
 - Anti-HBs > 10 mIU/mL
- Review hepatitis B vaccine schedules for dialysis patients
 - Recombinvax-HB 40 mcg
 - Series 1: mos 0, 1, 6
 - Series 2: if Anti-HBs < 10 after Series 1 (or falls < 10 after Series 1)
 - Booster if AntiHBs after Series 2 falls < 10
- Discuss Hepatitis B study at 2 major teaching hospitals in Vancouver
 - Response rate to vaccination:
 - Series 1: 61.4%; Series 2: 58.3%; Booster 81.8%
 - Factor(s) associated with poor response:
 - Non-adherence to vaccination regimen