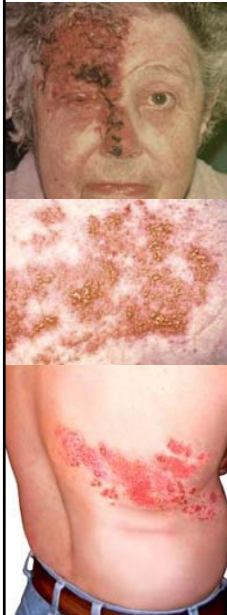


Automated surveillance for herpes zoster and postherpetic neuralgia using electronic health data

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Shingles - background



- Varicella zoster virus → chickenpox
- Virus dormant in the nervous system forever
- Can reactivate later in life → painful rash
 - ✓ Affects up to 1,000,000 Americans per year
- Usually resolves but complications in 10-20%
 - ✓ Prolonged pain (postherpetic neuralgia)
 - ✓ Ocular disease (keratitis / uveitis)
 - ✓ Motor neuropathy
 - ✓ Meningitis
 - ✓ Encephalitis

Forces impacting zoster incidence



Enabling factors

- Aging of the population
- Immune compromising conditions
- Immune compromising medications
- Varicella vaccine (short term)
 - ✓ ↓ immune boosting due to drop in circulating wild-type virus

Inhibiting factors

- Varicella vaccine (longterm)
- Shingles vaccine

NET IMPACT: UNKNOWN

Challenges in zoster surveillance

- Herpes zoster is not a notifiable disease
- Diagnosis often clinical rather than laboratory-based
 - ✓ Accuracy of diagnosis can be uncertain
 - ✓ Electronic laboratory surveillance systems of no benefit
- Studies of incidence labour intensive, expensive, time-limited; each new study begins again from scratch
- The primary morbidity associated with zoster is pain – an elusive outcome to detect and follow
 - ✓ Requires detailed chart review



Advantages of electronic health data

- Large databases already exist
- Large, diverse, distributed populations
- Rapid, efficient analysis possible
- Low marginal cost for repeated analyses

- But is it accurate?



Specific Aims

1. Develop an algorithm to detect herpes zoster incidence using electronic medical record data.
2. Develop an algorithm to detect postherpetic neuralgia using electronic medical record data.



An approach to developing algorithms for event detection in EMR data

1. Try to identify every case of interest within a defined population using a broad range of search criteria
 - Select criteria for maximal combined sensitivity (without regard to specificity)
2. Review a representative sample of charts
3. Calculate sensitivity and positive predictive value for each search criteria
4. Combine / modify search criteria to maximize sensitivity and positive predictive value



Population

- Harvard Vanguard Medical Associates
 - ✓ Large, multispecialty, multisite ambulatory practice
 - ✓ Based in Eastern Massachusetts
 - ✓ 550,000 patients
 - ✓ Comprehensive electronic medical record system (EPIC Systems) in place since 1996
 - ☞ Includes demographics, diagnoses, prescriptions, lab orders & results, vaccine administration

Detection of herpes zoster - search criteria

1	ICD9 053.x (any position, incident use, episode length=1year)
2	ICD9 for rash =782.1 AND prescription for antiviral within next 0-14 days NOT ICD9=053.x within -90 to +90 days
3	ICD9 for varicella = (052.7 or 052.8 or 052.9) AND age>50 NOT ICD9=053.x within -90 to +90 days
4	ICD9 for herpes simplex = (054.x) AND age>50 NOT ICD9=053.x within -90 to +90 days
5	Lab test for zoster (culture, DFA, PCR, IgM) NOT ICD9=053.x within -90 to +90 days

Herpes zoster incidence – search criteria

	Charts Flagged	Charts Reviewed
At risk (HVMA population, 2008)	557,708	267
ICD9 for zoster (any position)	2084	100
ICD9 for rash and antiviral Rx*	56	56
ICD9 for varicella and age >50*	11	11
ICD9 for herpes simplex and age >50*	785	50
Lab test for zoster*	165	50

*in cases WITHOUT an ICD9 for HZ

Chart review criteria

Definite case

- Herpes zoster is the MD's top diagnosis
- MD treated patient as such (by drug or observation)
- Tests and subsequent events do not reveal an alternative diagnosis

Possible case

- Herpes zoster is on the MD's differential but presentation atypical and reasonable alternatives on the differential
- Tests and subsequent events do not reveal an alternative diagnosis

Detection of incident herpes zoster - results

	Sensitivity	Positive Predictive Value
ICD9 for zoster (any position)	99%	88%
ICD9 for zoster (primary position)	88%	92%
ICD9 for rash and antiviral Rx*	0.1%	5.4%
ICD9 for varicella and age >50*	0.2%	36%
ICD9 for herpes simplex and age >50*	0%	0%
Lab test for zoster*	0.3%	4.0%

*in cases WITHOUT an ICD9 for HZ

Aim 2 - Detection of postherpetic neuralgia

- Study nested within the population of probable zoster patients identified through aim 1
 - ✓ Any patient with ICD9 = 053.x in 2008
 - ✓ N = 2089

Postherpetic neuralgia - search criteria

1	New analgesic Rx within 0-60 days of zoster ICD9
2	New anticonvulsant Rx within 0-60 days of zoster ICD9
3	New antidepressant Rx within 0-60 days of zoster ICD9
4	ICD9 053.1x (herpes zoster with nervous system complications)
5	Neuralgia ICD9 (729.2) within 0-180 days of zoster ICD9
6	Acute & chronic pain ICD9 (338.x) within 0-180 days of zoster ICD9
7	Generalized pain ICD9 (780.96) within 0-180 days of zoster ICD9
8	Two or more occurrences of zoster ICD9 (053.x)



Analgesics

ACETAMINOPHEN-CODEINE
 ACETAMINOPHEN-PAMABROM
 ACETAMINOPHEN-SALICYLAMIDE
 ASPIRIN-ACETAMINOPHEN
 ASPIRIN-CODEINE
 ASPIRIN-HYDROCODONE
 BROMFENAC
 BUPRENORPHINE
 BUTALBITAL-ACETAMINOPHEN
 BUTORPHANOL
 CELECOXIB
 CODEINE
 DICLOFENAC
 ETODOLAC
 FENTANYL
 HYDROCODONE
 HYDROMORPHONE
 IBUPROFEN
 INDOMETHACIN
 KETOPROFEN
 KETOROLAC

LEVOMETHADYL
 LEVORPHANOL
 LIDOCAINE GEL
 MECLOFENAMATE
 MEFENAMIC ACID
 MELOXICAM
 MEPERIDINE
 METHADONE
 MORPHINE
 NABUMETONE
 NALBUPHINE
 NAPROXEN
 OXYCODONE
 OXYMORPHONE
 PENTAZOCINE
 PIROXICAM
 PROPOXYPHENE
 ROFECOXIB
 SULINDAC
 TRAMADOL
 VALDECOXIB

Anticonvulsants

CARBAMAZEPINE
 DIVALPROEX
 GABAPENTIN
 LAMOTRIGINE
 LEVETIRACETAM
 OXCARBAZEPINE
 PHENYTOIN
 PREGABALIN
 TOPIRAMATE
 VALPROIC ACID

Antidepressants

AMITRIPTYLINE
 BUPROPION
 DESIPRAMINE
 DESVENLAFAXINE
 DOXEPIN
 DULOXETINE
 ESCITALOPRAM
 FLUOXETINE
 FLUVOXAMINE
 IMPRAMINE
 LOXAPINE
 MAPROTILINE
 NEFAZODONE
 NORTRIPTYLINE
 PAROXETINE
 PROMAZINE
 PROTRIPTYLINE
 SERTRALINE
 TRAZODONE
 TRIMIPRAMINE
 VENLAFAXINE



Chart review criteria

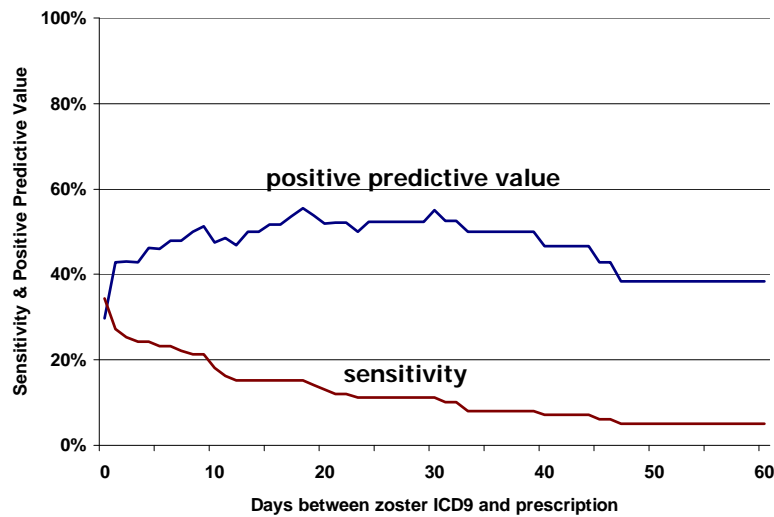
- Postherpetic neuralgia defined as persistent pain ≥ 30 days from herpes zoster onset
 - ✓ Zoster onset date from chart review
- 2089 patients with ICD9 for zoster in 2008
 - ✓ 779 patients fulfilled search criteria for PHN
 - ✓ 438 charts pulled
 - ✓ 257 reviewed thus far
 - ✓ 99 confirmed cases of PHN
 - ☞ corresponds to ~12% rate of PHN in the full population

Study	Setting	PHN
Choo et al. 1997	New England	8%
Yawn et al. 2007	Olmsted County	18%

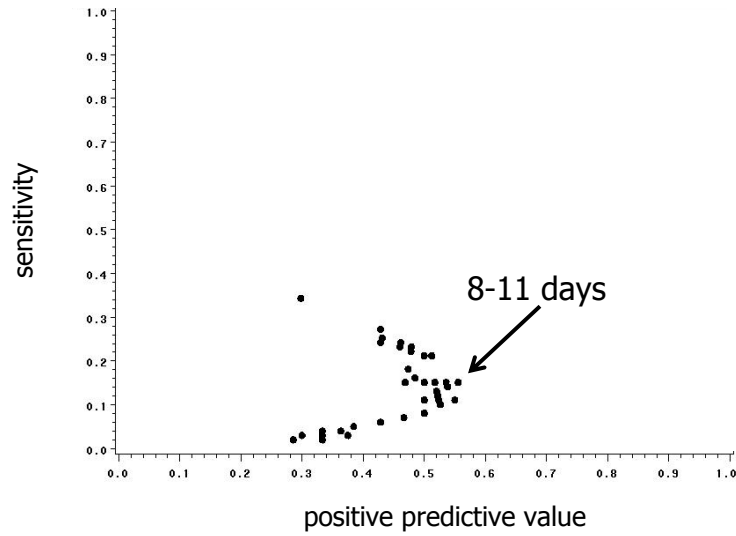
Postherpetic neuralgia - results

Criteria	Sensitivity	Positive Predictive Value
New analgesic Rx within 0-60 days	43%	29%
New anticonvulsant Rx within 0-60 days	55%	69%
New antidepressant Rx within 0-60 days	21%	44%
ICD9 053.1x (HZ nervous system comp)	62%	90%
Neuralgia ICD9 within 0-180 days	13%	87%
Acute & chronic pain ICD9 within 0-180 days	4%	50%
Generalized pain ICD9 within 0-180	0%	NA
Two or more zoster ICD9's ≥ 30 days apart	69%	69%

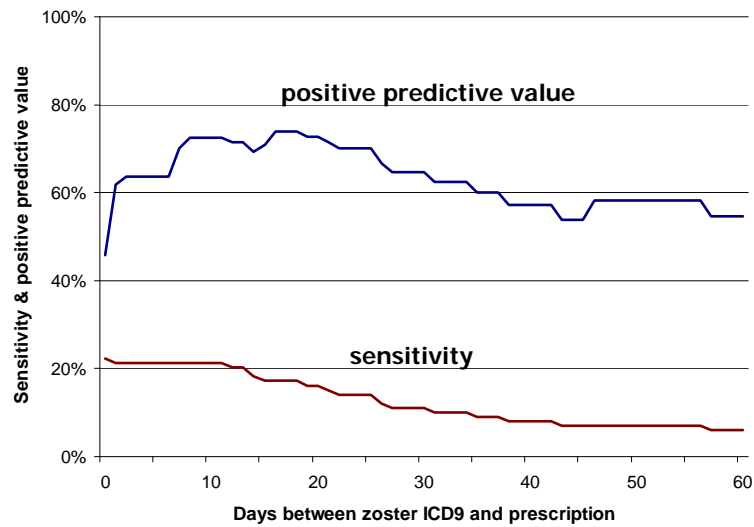
Sensitivity and positive predictive value for PHN as function of interval from first zoster ICD9 to first analgesic prescription



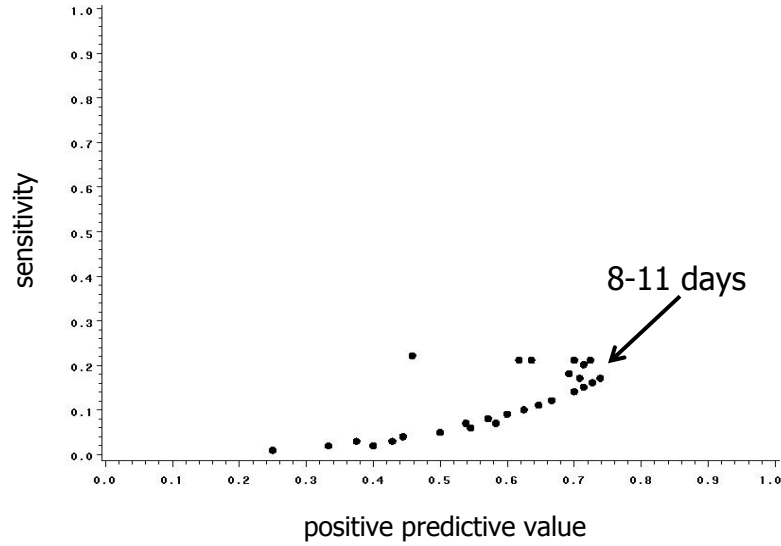
Analgesic interval receiver-operator curve



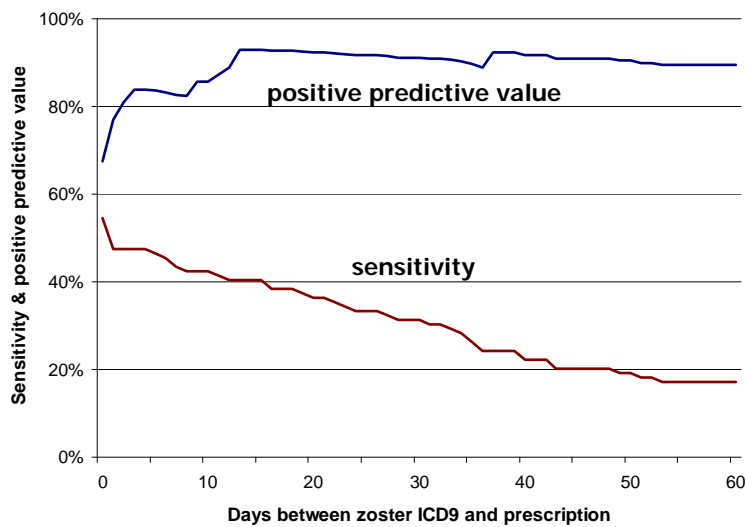
Sensitivity and positive predictive value for PHN as function of interval from first zoster ICD9 to first antidepressant prescription



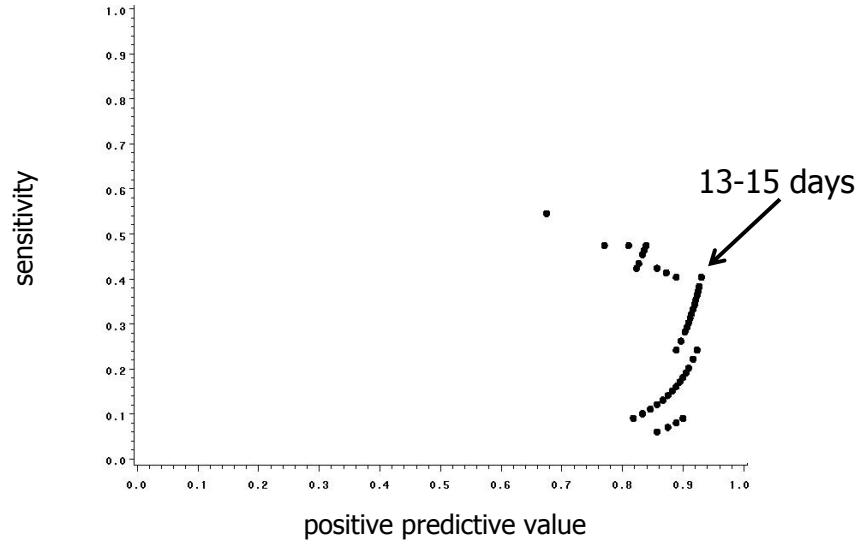
Antidepressant interval receiver-operator curve



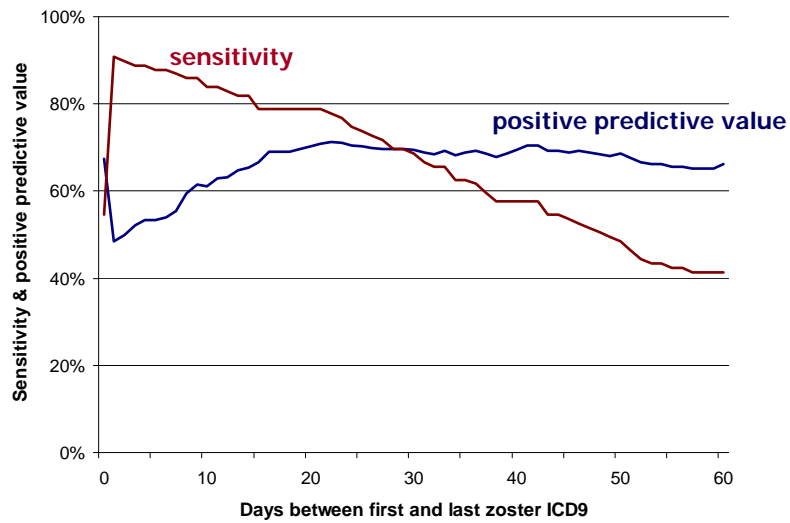
Sensitivity and positive predictive value for PHN as function of interval from first zoster ICD9 to first anticonvulsant prescription



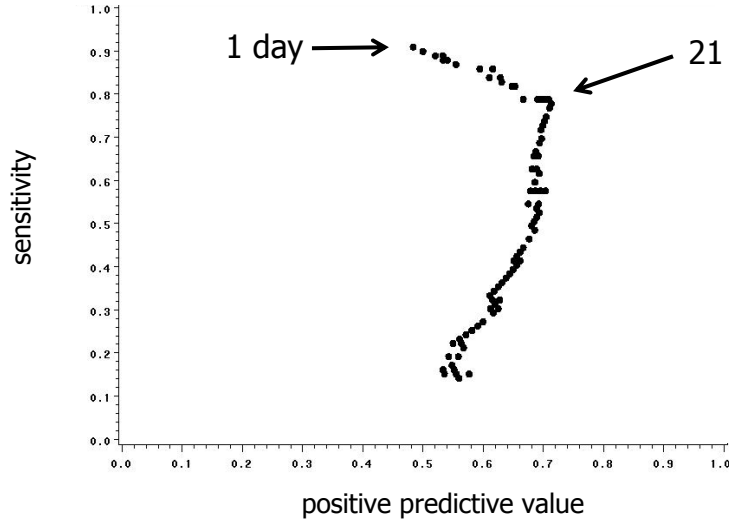
Anticonvulsant interval receiver-operator curve



Sensitivity and positive predictive value for PHN as function of interval from first zoster ICD9 to last zoster ICD9



Visit interval receiver-operator curve



Postherpetic neuralgia – combining terms visit interval + medications

Criteria	Sensitivity	Positive Predictive Value
Two or more visits ≥ 21 days apart	79%	71%
Two or more visits ≥ 21 days apart AND new Rx for anticonvulsant	44%	98%
Two or more visits ≥ 21 days apart AND new Rx for anticonvulsant or antidepressant	51%	91%
Two or more visits ≥ 21 days apart AND new Rx for anticonvulsant or antidepressant or analgesic	63%	89%

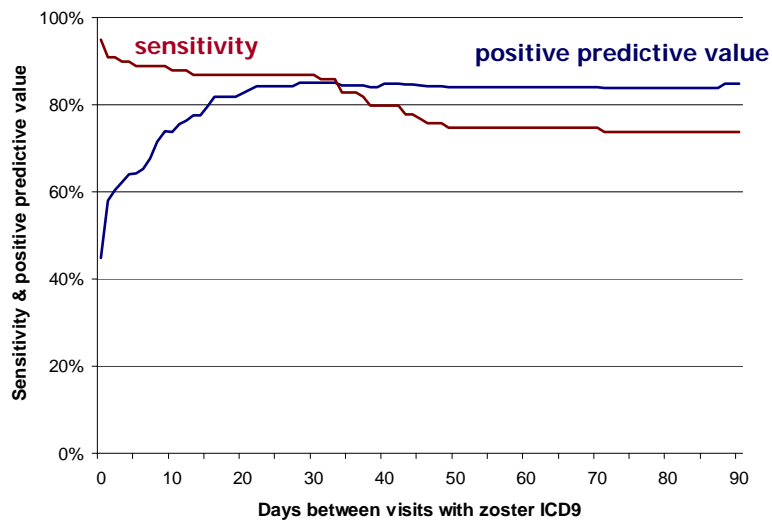


Postherpetic neuralgia – combining terms visit interval, medications and neuro ICD9's

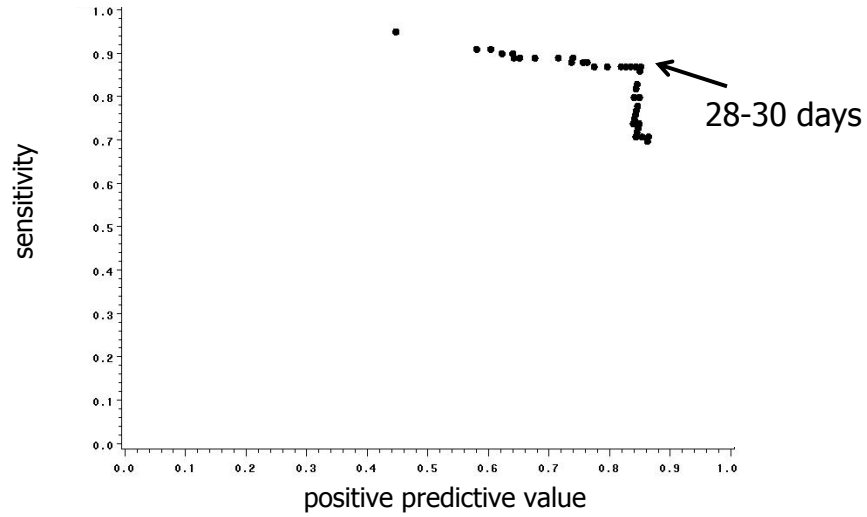
Criteria	Sensitivity	Positive Predictive Value



Sensitivity and positive predictive value for PHN as function of interval from first zoster ICD9 to last zoster ICD9



Combination equation receiver-operator curve (varying visit interval)



Postherpetic neuralgia – combining terms

Two or more visits ≥ 30 days apart AND new Rx for anticonvulsant or antidepressant or analgesic
 OR
 ICD9 053.1x (HZ nervous system complication)
 OR
 ICD9 for neuralgia 0-180 days after zoster ICD9

Sensitivity: 87%
 Positive predictive value: 85%

Limitations

- Preliminary analysis
 - ✓ Need to complete chart reviews and adjust for sampling strategy
- Algorithms developed from a single year of data from a single medical system via retrospective chart review
 - ✓ Coding practices may vary over time and from practice to practice
 - ✓ Algorithms will need to re-validated for new settings

Summary

- Incident zoster
 - ✓ ICD9 053.x (any position)
 - ✓ sensitivity 99%, PPV 88%
- Incident postherpetic neuralgia
 - ✓ Combination equation including visit interval, medication prescriptions, and selected ICD9 codes
 - ✓ Sensitivity 87%, PPV 85%
- In process:
 - ✓ Completion of chart reviews, adjustment for sampling, re-validation
- Structured combinations of electronic health information can identify elusive outcomes with high sensitivity and positive predictive value
 - ✓ Rigorous algorithm development and validation critical for reliability



Thank you

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- Julie Dunn
- Katherine Yih
- Peter Choo

Discussion Welcome!

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