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Effective Prevention: Identifying Those at Greatest Risk

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Injury Definition?

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- **Any injury**
  - Including concussion, contusion, and/or laceration
- **Any musculoskeletal injury**
  - Including fracture, dislocation, and/or overuse syndrome
- **Any acute joint sprain or muscle strain**
  - Including upper extremity, core, and/or lower extremity
    - Excluding wrist, hand, and finger injury
- **Any "time-loss" joint sprain or muscle strain**
  - Complete restriction of activity for 1 or more days

Injury Risk Screening

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Demographics (Potential Confounders)
Sport; Gender; Prior Injury; Game Exposure

Movement Efficiency Ratings
Functional Movement Screen (FMS); Fusionetics

Postural Balance
Y-Balance Test; BESS

Core Muscle Endurance (Hold Time)
Back Extension; Prone Plank, Side Plank, Wall Sit

Muscle Strength/Power (Asymmetry)
Dynamometry; Single-Leg Vertical/Broad Jump

Dynamic Movement Tests
Landing Error Scoring System; Hop Tests; Closed Kinetic Chain Upper Extremity Stability (CKCUES)

Muscle Flexibility/Joint Mobility
Sit-Reach; Beighton Scale

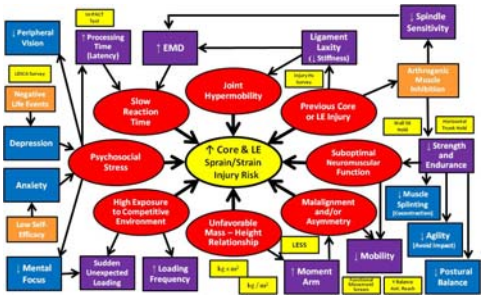
Anthropometric Measures
Height; Body Mass Index; Estimated Mass Moment of Inertia

Neurocognitive/Visuomotor Tests
ImPACT; CogSport; Erikson Flanker Test; Dynavision

Self-Reported Status (Surveys)
Life Events Survey for Collegiate Athletes; Sport Fitness Index; Center for Epidemiological Studies – Depression (CES-D); Pittsburgh Sleep Quality Index

Wearable Sensors
Inertial Measurement Units; HR Monitors

Interrelationships Among Determinants of Risk for Injury, Re-injury, & Chronic Disability



Injury Prediction

5

- Not everyone believes it's possible –
  - Why screening tests to predict injury do not work – and probably never will…: a critical review.
    - Bahr R, 2016, *Br J Sports Med*
  - Return to play and physical performance tests: evidence-based, rough guess or charade?
    - Hegedus EJ & Cook CE, 2015, *Br J Sports Med*
  - Predicting future physical injury in sports: it's a complicated dynamic system.
    - Cook C, 2016, *Br J Sports Med*

Quantification of Injury Risk Level

6

- Considerations for interpretation of research findings:
  1. **Outcome** (Injury Definition)
     - Location (UE, Core, LE) – Severity – Type (Acute, Overuse)
  2. **Population** (Injury Incidence – Pre-Test Probability)
     - Gender – Age – Sport – Position – Level of Competition
  3. **Predictor** (Single Risk Factor or Composite Indicator)
     - Value derived from single test or a battery of screening tests?
     - Univariable vs. Multivariable Analysis (Adjusted Effect Estimates)
  4. **Duration of surveillance period**
     - Injury incidence progressively increases over time
- Prediction accuracy (validity) depends heavily on:
  - Number of criterion-positive (injured) cases within cohort
    - Minimum 10 positive cases per variable included in prediction model

Terminology

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- **Correlation and Analysis of Variance:**
  - **Bivariate:** 2 continuous variables (X and Y)
  - **Multivariate:** Multiple DVs (Ys) and IVs (Xs)
- **Exposure-Outcome Association:**
  - **Univariable:** 1 predictor (X) of binary outcome (Y)
    - Predictive variable may be continuous or binary
  - **Multivariable:** ≥2 predictors of binary outcome (Y)
    - Predictive variables may be continuous or binary

Univariable 2 X 2 Cross-Tabulation

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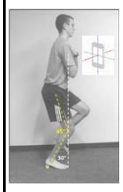
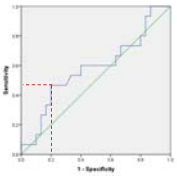
- **Receiver Operating Characteristic (ROC) Analysis**
  - Continuous variable converted to binary classification
  - Cut-point selected to optimize overall prediction accuracy





RMS*	Injury	No Injury	Incidence
≥ .06	7	6	54%
< .06	8	24	25%
Total	15	30	

Sensitivity 47% Specificity 80%

$\chi^2(1)=3.46$ 1-Sided $P=.067$

RR=2.15 90% CI: 1.12 – 4.16

OR=3.50 90% CI: 1.13 – 10.89

* Root Mean Square of Instantaneous Change in Body Mass Acceleration (Jerk)

What is the level of injury risk?

- **Risk Ratio (RR)**: Comparison of Injury Incidence
  - Hi-Risk Proportion Injured / Lo-Risk Proportion Injured
- **Odds Ratio (OR)**: Comparison of Occurrence vs. Non-Occurrence
  - Hi-Risk Injury Odds / Lo-Risk Injury Odds
- **Hazard Ratio (HR)**: Comparison of Instantaneous Injury Rates
  - Hi-Risk Slope / Lo-Risk Slope (Injuries per athlete per unit of time)

Association	RR	HR	OR
Small	≥ 1.1	≥ 1.3	≥ 1.5
Moderate	≥ 1.4	≥ 2.0	≥ 3.4
Large	≥ 2.0	≥ 4.0	≥ 9.0
Very Large	≥ 3.3	≥ 10.0	≥ 32.0

Hopkins WG. Sportscience. 2010;14:49-58 (sportssci.org/2010/wghlinmod.htm).
Hopkins WG. In: Verhagen E, van Mechelen W (eds.). *Sports Injury Research*. 2010.

Assessment of Predictive Validity

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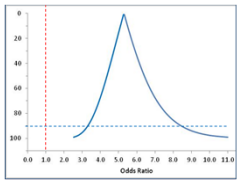
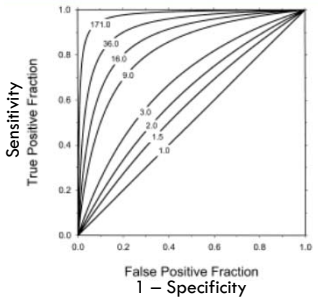
1. Magnitude of Effect Size Ratio (RR, HR, and/or OR)
2. Confidence Interval Lower Limit > vs. ≤ 1.0
   - 90% CI: 5% expected frequency of values ≤ LL
     - Equivalent to one-sided test of statistical significance



Odds Ratio = 5.28 (90% CI: 3.31 – 8.44)

Limitations of the Odds Ratio

A given value for an Odds Ratio can be derived from many different combinations of values for Sensitivity and 1 – Specificity



Pepe MS, et al. Limitations of the odds ratio in gauging the performance of a diagnostic, prognostic, or screening marker. *Am J Epidemiol*. 2004;159(9):882-890.

Univariable 2 X 2 Cross-Tabulation

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- **Sensitivity and Specificity**
  - Probability that outcome status will be correctly classified by test result
- **Positive and Negative Predictive Value (PPV and NPV)**
  - Probability that a test will correctly classify an individual as having high-risk vs. low-risk status
- **Positive and Negative Likelihood Ratio (+LR and –LR)**
  - Magnitude of increase (+) or decrease (–) in odds for injury occurrence on the basis of classification as high-risk vs. low-risk status

RMS*	Injury	No Injury	Incidence		
≥ .06	7	6	54%	PPV=54%	+LR=2.33
< .06	8	24	25%	NPV=75%	–LR=0.67
Total	15	30			
	Sensitivity 47%	Specificity 80%			

Univariable Cross-Tabulation Analysis

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	Outcome Positive	Outcome Negative	Total	Incidence (Post-Test Prob)		
Predict Positive	True Positive	False Positive	TP+FP	TP/(TP+FP)	+LR= Sens/1-Spec	PPV= TP/(TP+FP)
Predict Negative	False Negative	True Negative	FN+TN	FN/(FN+TN)	-LR= 1-Sens/Spec	NPV= TN/(FN+TN)
Total	TP+FN	FP+TN	TP+TN+ FP+FN	Risk Ratio= Incidence/Incidence	Odds Ratio= +LR/-LR	
Pre-Test Prob= Outcome(+)/Total	Sensitivity= TP/(TP+FN)	Specificity= TN/(TN+FP)				

Advantage of Likelihood Ratios

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Example: N=100; 80% Sensitivity; 80% Specificity

+LR = Sensitivity/1– Specificity
–LR = 1–Sensitivity/Specificity

+LR = .80/.20 = 4.00
–LR = .20/.80 = 0.25

OR = +LR/ –LR

OR = 4.00/0.25 = 16.00

Incidence	Injury	No Injury	
10%	8	18	PPV=31%
	2	72	NPV=97%
30%	24	14	PPV=63%
	6	56	NPV=90%
50%	40	10	PPV=80%
	10	40	NPV=80%
70%	56	6	PPV=90%
	14	24	NPV=63%
90%	72	2	PPV=97%
	18	8	NPV=31%

Key Concepts

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- **"Exposure"**
  1. Volume of participation in activity presenting injury risk
     - Athlete-Exposures (AEs): Number of practices and games
  2. Any factor associated with outcome (predictive variable)
- **"Confounding"**
  - Unequal "exposure" within groups that are compared
    - Gender, Sport, Position, Experience, Injury History, Starter Status
  - Example: High performance on screening test of agility associated with injury occurrence
    - Starters possess good agility + exposed to greater injury risk

Key Concepts

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- **"Interaction"**
  - Observed effect between 2 or more predictive factors that is > or < than either one acting independently
- **Identification of confounding and interactions:**
  1. Stratified univariable analyses – comparison of odds ratios
     - Breslow-Day test for homogeneity of odds ratios ($P > .10$)
  2. Multivariable analysis (Logistic Regression; Cox Regression)
     - Effect of a given predictor adjusted for the effects of one or more other predictors (confounding factors must be included)
     - Interaction term (Factor A X Factor B) must be included to quantify its effect

Development of a Prediction Model

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1. Process begins with univariable analyses
   - Selection of factors to include in multivariable analysis
     - One-sided test appropriate when focus is whether or not a point estimate exceeds a specified value (e.g., ratio > 1.0)
     - Screening criterion as large as one-sided $P < .20$ or .25
2. Multivariable analysis identifies best set of predictors
   - Entry of binary variables permits comparison of univariable ORs to "adjusted" multivariable ORs
     - Logistic regression output: EXP(B) = Adjusted OR
3. Prediction accuracy assessed by univariable analysis
   - Multivariable model converted to binary classification
     - High-Risk vs. Low-Risk status

Continuous Variables vs. Binary Categories (Risk Factor + or –)

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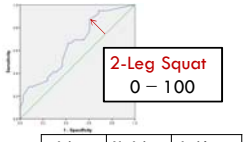
- Binary Categories: High Risk vs. Low Risk
  - Cut-point determined by ROC analysis

N=77
Core or LE Injury
39 Injured: 51%

	Injury	No Injury	Incidence
≥ 289	20	4	83%
< 289	19	34	36%
Total	39	38	

Sensitivity= 51% Specificity= 90%

+LR = 5.30 –LR = 0.49 **OR = 8.95**



	Injury	No Injury	Incidence
≤ 83	34	23	60%
> 83	5	15	25%
Total	39	38	

Sensitivity= 87% Specificity= 40%

+LR = 1.44 –LR = 0.33 **OR = 4.44**

Logistic Regression

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- Natural log (ln) of "odds" for event occurrence
  - Odds = Probability / 1 – Probability
  - Probability = Odds / 1 + Odds
- $\ln(P/1-P) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots$
  - ln base e = 2.718
    - $e^1 = e$; ln(e) = 1
    - e^{β} = EXP(B) = change in odds for 1-unit increase in X
- For a binary predictive variable (0, 1):
  - EXP(B) = "Adjusted" Odds Ratio
    - Adjusted for the effects of other predictors included in model

Continuous Variables vs. Binary Categories (Risk Factor + or –)

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- Entry as continuous variables:

N=77
Core or LE Injury
39 Injured: 51%

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	90% C.I.for EXP(B) Lower	Upper
Step 1[a]	Score2LS	-.046	.019	5.844	1	.016	.955	.925	.985
	Plays	.003	.001	7.813	1	.005	1.003	1.001	1.005
	Constant	2.750	1.397	3.876	1	.049	15.639		

a. Variable(s) entered on step 1: Score2LS, Plays.

- Model χ^2 (2) = 16.98; $P < .001$; Nagelkerke R^2 = .264

- Entry as categorical variables:

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	90% C.I.for EXP(B) Lower	Upper
Step 1[a]	HiGameExp(1)	1.985	.631	9.891	1	.002	7.278	2.577	20.550
	Lo2LS_83.33(1)	1.102	.623	3.131	1	.077	3.009	1.081	8.379
	Constant	-1.354	.550	6.066	1	.014	.258		

a. Variable(s) entered on step 1: HiGameExp, Lo2LS_83.33.

Univariable ORs
8.95
4.44

- Model χ^2 (2) = 9.77; P = .008; Nagelkerke R^2 = .285

Continuous Variables vs. Binary Categories (Risk Factor + or –)

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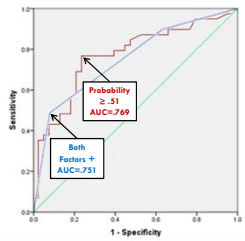
$\ln(P/1-P) = \beta_0 + \beta_1 X_1 + \beta_2 X_2$



Probability	Injury	No Injury	% Injured
≥ .51	29	9	76%
.00 - .50	10	29	26%
Total	39	38	RR = **2.98**

Fisher's Exact One-Sided $P < .001$
Sensitivity= 74% Specificity= 76%
OR = **9.34** (90% CI: 3.91 – 22.32)

Factors +	Injury	No Injury	% Injured
Both	19	3	86%
0 or 1	20	35	36%
Total	39	38	RR = **2.38**

Fisher's Exact One-Sided $P < .001$
Sensitivity= 49% Specificity= 92%
OR = **11.08** (90% CI: 3.61 – 34.01)

N=77
Core or LE Injury
39 Injured: 51%

Inertial Measurement Unit (IMU)

22

Utilization of Practice Session Average Inertial Load to Quantify College Football Injury Risk

Gary B. Wilkerson,[1] Ashish Gupta,[2] Jeff R. Allen,[2] Clay M. Keith,[2] and Marisa A. Colston[1]

$$\text{Plyr Load} = \sqrt{\left(fwd_{t=i+1} - fwd_{t=i}\right)^2 + \left(side_{t=i+1} - side_{t=i}\right)^2 + \left(up_{t=i+1} - up_{t=i}\right)^2}$$

fwd : forward acceleration
side : sideways acceleration
up : upwards acceleration
t : time

High Player Load value =
High Rate of Change in Acceleration
- Forward – Backward
- Right – Left
- Up – Down

Continuous Variables vs. Binary Categories (Risk Factor + or –)

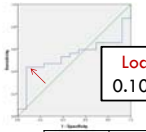
23

- Binary Categories: High Risk vs. Low Risk
  - Cut-point determined by ROC analysis

N=45
UE, Core, or LE Injury
32 Injured: 71%

	Injury	No Injury	Incidence
≥ 289	22	3	88%
< 289	10	10	50%
Total	32	13	

Sensitivity= 69% Specificity= 77%
+LR = 4.13 –LR = 0.38 **OR = 7.33**



	Injury	No Injury	Incidence
≤ 0.15	13	1	93%
> 0.15	19	12	61%
Total	32	13	

Sensitivity= 41% Specificity= 92%
+LR = 5.28 –LR = 0.64 **OR = 8.21**

Continuous Variables vs. Binary Categories (Risk Factor + or –)

24

- Entry as continuous variables:

N=45
UE, Core, or LE Injury
32 Injured: 71%

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	90% C.I.for EXP(B) Lower	Upper
Step 1[a]	LoadCoV	1.987	7.210	.076	1	.783	7.295	.000	1031842.600
	Plays	.003	.001	3.672	1	.055	1.003	1.000	1.005
	Constant	-.339	1.440	.055	1	.814	.712		

a. Variable(s) entered on step 1: LoadCoV, Plays.

- Model χ^2 (2) = 4.35; P = .114; Nagelkerke R^2 = .132

- Entry as categorical variables:

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	90% C.I.for EXP(B) Lower	Upper
Step 1[a]	HiPlays_289(1)	1.854	.789	5.520	1	.019	6.386	1.744	23.388
	LoCoV_15(1)	1.906	1.145	2.774	1	.096	6.726	1.024	44.225
	Constant	-.331	.495	.448	1	.503	.718		

a. Variable(s) entered on step 1: HiPlays_289, LoCoV_15.

Univariable ORs
7.33
8.21

- Model χ^2 (2) = 11.80; P = .003; Nagelkerke R^2 = .330

Continuous Variables vs. Binary Categories (Risk Factor + or −)

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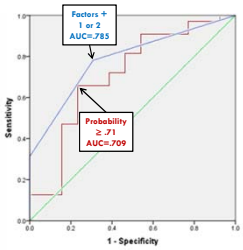
$\ln(P/1-P) = \beta_0 + \beta_1 X_1 + \beta_2 X_2$



N=45
UE, Core, or LE Injury
32 Injured: 71%

Probability	Injury	No Injury	% Injured
≥ .71	21	3	88%
.00 - .70	11	10	52%
Total	32	13	RR = 1.67

Fisher's Exact One-Sided $P < .011$
Sensitivity= 66% Specificity= 77%
OR = 6.36 (90% CI: 1.83 – 22.08)

Factors +	Injury	No Injury	% Injured
1 or 2	25	4	86%
0	7	9	44%
Total	32	13	RR = 1.97

Fisher's Exact One-Sided $P < .004$
Sensitivity= 78% Specificity= 69%
OR = 8.04 (90% CI: 2.39 – 27.03)

Univariable Results – Possible Interactions

26

	Variable	Cut-Point	P*	OR	OR 90% CI
A	Game Exposure (Plays)	≥ 289	< .001	8.46	2.78, 25.72
	Movement Efficiency Score	≤ 82.75	.025	3.16	1.32, 7.58
B	2-Leg Squat	≤ 83.33	.014	3.71	1.51, 9.13
C	2-Leg Squat - Heel Lift	≤ 93.89	.060	2.63	1.07, 6.47
D	1-Leg Squat	≤ 79.16	.005	8.41	2.17, 32.59
E	Concussion History	≥ 1	.074	2.84	1.01, 7.98
F	Position Category (Back/Line)	†	.355	1.33	0.61, 2.90

* Fisher's Exact One-Sided Test
† Reference Category = Offensive or Defensive Back Position

6 Factors = 15 2-Way Interactions

A X B B X C C X D D X E E X F
A X C B X D C X E D X F
A X D B X E C X F
A X E B X F
A X F

N=77
UE, Core, or LE Injury
45 Injured: 58%

Interaction Effect

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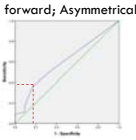
- **2-Leg Squat with Heel Lift (2LS-HL)**
  - Foot turns out or flattens; Knee valgus or varus; Trunk forward lean; Lumbo-pelvic arching or rounding; Arms fall forward; Asymmetrical weight shift

	Injury	No Injury	Incidence
≤ 94	17	6	74%
> 94	28	26	52%
Total	45	32	

Sensitivity= 38% Specificity= 81%
+LR = 2.02 –LR = 0.77 **OR = 2.63**



N=77
UE, Core, or LE Injury
45 Injured: 58%

- **Position Category**
  - Back: QB, RB, WR, LB, DB, ST
  - Line: OC, OG, OT, TE, DG, DT, DE

	Injury	No Injury	Incidence
Back	20	12	63%
Line	25	20	56%
Total	45	32	

Sensitivity= 44% Specificity= 63%
+LR = 1.10 –LR = 0.89 **OR = 1.33**

Interaction Effect: 2LS-HL X Position Category

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N=77
UE, Core, or LE Injury
45 Injured: 58%

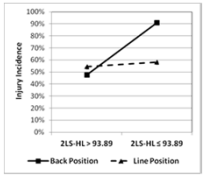
Line	Injury	No Injury	Incidence
≤ 94	7	5	58%
> 94	18	15	55%
Total	25	20	

Sensitivity= 28% Specificity= 75%
+LR = 1.12 –LR = 0.96 **OR = 1.17**

Back	Injury	No Injury	Incidence
≤ 94	10	1	91%
> 94	10	11	48%
Total	20	12	

Sensitivity= 50% Specificity= 92%
+LR = 6.00 –LR = 0.55 **OR = 11.00**

- Breslow-Day Test (Homogeneity of ORs)
  - $P = .074$



Final Prediction Models

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N = 77
1. Game Plays ≥ 289
2. 1LS ≤ 79
3. Back X 2LS-HL ≤ 94

Factors +	Injury	No Injury	Incidence	
≥ 2	28	2	93%	+LR=9.96
0 or 1	17	30	36%	–LR=0.40
Total	45	32		

Sensitivity= 62% Specificity= 94%
OR = 24.71 (90% CI: 6.71, 90.96)

N = 39
1. Game Plays ≥ 289
2. 1LS ≤ 79
3. Back X 2LS-HL ≤ 94
4. Inertial Load CoV ≤ .15

Factors +	Injury	No Injury	Incidence	
≥ 2	23	2	92%	+LR=5.75
0 or 1	3	11	21%	–LR=0.14
Total	26	13		

Sensitivity= 88% Specificity= 85%
OR = 42.17 (90% CI: 8.36, 212.67)

Cox Regression

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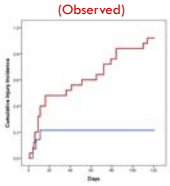
- Time-to-event analysis (survival analysis)
  - **Hazard**: Probability that an individual will experience outcome event with specified time interval
  - **Hazard Ratio**: Comparison of instantaneous risk for injury at any point during specified time interval
  - **Cumulative Hazard**: Number of events expected by the end of the specified time interval (if repeatable)
  - **Cumulative Injury Incidence**: Proportion of group members who have experienced outcome event at successive time points

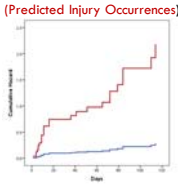
Cox Regression – Binary Prediction

N = 39 4-Factor Prediction Model
≥ 2 Positive Factors vs. 0 or 1 Positive Factor
HR = 7.70 (90% CI: 2.75, 21.57)

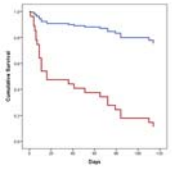
Cumulative Injury Incidence
(Observed)



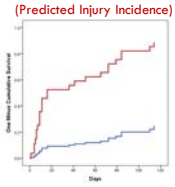
Cumulative Hazard
(Predicted Injury Occurrences)



Cumulative Survival
(Predicted Injury Avoidance)



1 – Cumulative Survival
(Predicted Injury Incidence)



Bahr R, *Br J Sports Med.* 2016

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- Why screening tests to predict injury do not work – and probably never will…. a critical review.
  - At least 3 steps needed to validate a screening test:
    1. A strong relationship must be established between the test result (dichotomous categories) and injury risk
    2. Validate the relationship in multiple cohorts (same criteria for high risk classification)
    3. Document that an intervention is more beneficial for athletes with high risk than the general athletic population (high risk + low risk)

Retrospective-Prospective Analyses of Screening Test Results

- Retrospectively-derived cut-points used to prospectively classify high vs. low risk

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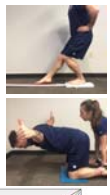
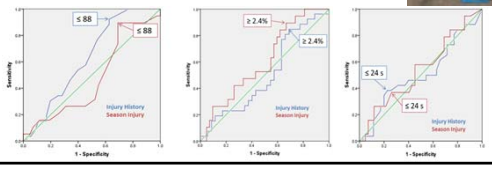
High School Football Players N=61

3-Factor Model					
		Previous Injury		Season Injury	
Factor	Cut	OR	Exp(B)	OR	Exp(B)
SFI	≤ 88	4.53	4.42	2.39	1.82
Y-AR%Diff	≥ 2.4	2.52	1.40	3.81	2.92
HTH (s)	≤ 24	2.11	2.23	1.64	1.45
Factors +	≥ 2	3.67	-	5.23	-





Summary

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- Model components and cut-points are highly specific to injury definition and cohort characteristics
- Persisting effects of prior injury and volume of exposure to high-risk conditions are potential confounders
- Any strong interactions between potential predictors should be identified and included in multivariable analysis
- Likelihood ratios are better indicators of screening test classification accuracy than PPV and NPV
- Time-to-event analysis of a binary risk classification model may augment evidence of its predictive validity
- Precision of an estimate of exposure-outcome association (RR, HR, or OR) is reflected by confidence interval limits

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