

# Package ‘MSoutcomes’

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**Title** CORE Multiple Sclerosis Outcomes Toolkit

**Version** 0.2.1

**Description** Enable operationalized evaluation of disease outcomes in multiple sclerosis. ‘MSoutcomes’ requires longitudinally recorded clinical data structured in long format. The package is based on the research developed at Clinical Outcomes Research unit (CORE), University of Melbourne and Neuroimmunology Centre, Royal Melbourne Hospital. Kalincik et al. (2015) <[doi:10.1093/brain/awv258](https://doi.org/10.1093/brain/awv258)>. Lorscheider et al. (2016) <[doi:10.1093/brain/aww173](https://doi.org/10.1093/brain/aww173)>. Sharmin et al. (2022) <[doi:10.1111/ene.15406](https://doi.org/10.1111/ene.15406)>. Dzau et al. (2023) <[doi:10.1136/jnnp-2023-331748](https://doi.org/10.1136/jnnp-2023-331748)>.

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CDEseq	<i>Identification of confirmed and sequential disability worsening and improvement events</i>
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### Description

Identify sequential disability worsening and improvement events confirmed over a specified time period, using roving baseline EDSS. The identification of events is based on clinical visit records, with each record including entries for patient code, visit date, EDSS score, and days since the most recent relapse. If a baseline EDSS score is not provided, it is determined as the first EDSS score recorded in the dataset outside 30 days (the default) of a relapse. Following a confirmed disability worsening or improvement event, the minimum EDSS score within the confirmation period, regardless of the recency of a relapse, becomes the new baseline EDSS score.

### Usage

```
CDEseq(Visits, mconf = 3 * 30.25, tRelapse = 30)
```

### Arguments

Visits	A data frame consisting of 6 columns: ID, dateEDSS, EDSS, daysPostRelapse (days since most recent relapse), bEDSS (baseline EDSS score), base.date (date of bEDSS).
mconf	Confirmation period (days) for EDSS worsening or improvement.
tRelapse	Minimum time in days since the most recent relapse to EDSS assessment.

### Value

A data frame.

### References

Sharmin, et al. European Journal of Neurology 2022;29(8):2321-2334.

**Examples**

```
data(SampleData)
output<-CDEseq(SampleData)
```

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**CDI***Identification of confirmed disability improvement events*

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**Description**

Identify disability improvement events confirmed over a specified time period. The identification of events is based on clinical visit records, with each record including entries for patient code, visit date, EDSS score, and days since the most recent relapse. If a baseline EDSS score is not provided, it is determined as the first EDSS score recorded in the dataset outside 30 days (the default) of a relapse. Following a confirmed disability improvement event, the minimum EDSS score within the confirmation period, regardless of the recency of a relapse, becomes the new baseline EDSS score. By default, only identify those improvement events that are sustained for the remainder of the follow-up.

**Usage**

```
CDI(Visits, mconf = 3 * 30.25, tRelapse = 30, sustained = TRUE)
```

**Arguments**

Visits	A data frame consisting of 6 columns: ID, dateEDSS, EDSS, daysPostRelapse (days since most recent relapse), bEDSS (baseline EDSS score), base.date (date of bEDSS).
mconf	Confirmation period (days) for EDSS improvement.
tRelapse	Minimum time in days since the most recent relapse to EDSS assessment.
sustained	If TRUE, the default, identifies only those EDSS improvement events sustained for the remaining recorded follow-up.

**Value**

A data frame.

**References**

Kalincik, et al. Brain 2015;138(11):3287-3298.

**Examples**

```
data(SampleData)
output<-CDI(SampleData)
```

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CDW

*Identification of confirmed disability worsening events*

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### Description

Identify disability worsening events confirmed over a specified time period. The identification of events is based on clinical visit records, with each record including entries for patient code, visit date, Expanded Disability Status Scale (EDSS) score, and days since the most recent relapse. If a baseline EDSS score is not provided, it is determined as the first EDSS score recorded in the dataset outside 30 days (the default) of a relapse. Following a confirmed disability worsening event, the minimum EDSS score within the confirmation period, regardless of the recency of a relapse, becomes the new baseline EDSS score. By default, only identify those worsening events that are sustained for the remainder of the follow-up.

### Usage

```
CDW(Visits, mconf = 3 * 30.25, tRelapse = 30, sustained = TRUE)
```

### Arguments

Visits	A data frame consisting of 6 columns: ID, dateEDSS, EDSS, daysPostRelapse (days since most recent relapse), bEDSS (baseline EDSS score), base.date (date of bEDSS).
mconf	Confirmation period (days) for EDSS worsening.
tRelapse	Minimum time in days since the most recent relapse to EDSS assessment.
sustained	If TRUE, the default, identifies only those EDSS worsening events sustained for the remaining recorded follow-up.

### Value

A data frame.

### References

Kalincik, et al. Brain 2015;138(11):3287-3298.

### Examples

```
data(SampleData)
output<-CDW(SampleData)
```

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PIRA	<i>Identification of progression independent of relapse activity (PIRA) events</i>
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### Description

Identify progression independent of relapse activity (PIRA) events confirmed over a specified time period. The identification of events is based on clinical visit records, each record including entries for patient code, visit date, EDSS score, and days since most recent relapse. If a baseline EDSS score is not provided, it is determined as the first EDSS score recorded in the dataset outside 30 days (the default) of a relapse. Following a confirmed PIRA event, the minimum EDSS score within the confirmation period, regardless of the recency of a relapse, becomes the new baseline EDSS score. Following a relapse, the first EDSS score recorded in the dataset outside 30 days (the default) of a relapse, becomes the new baseline EDSS score. By default, identify PIRA events that are sustained for the remainder of the follow-up.

### Usage

```
PIRA(Visits, mconf = 3 * 30.25, tRelapse = 30, sustained = TRUE)
```

### Arguments

Visits	A data frame consisting of 6 columns: ID, dateEDSS, EDSS, daysPostRelapse (days since most recent relapse), bEDSS (baseline EDSS score), base.date (date of bEDSS).
mconf	Confirmation period (days) for EDSS progression.
tRelapse	Minimum time in days since the most recent relapse to EDSS assessment.
sustained	If TRUE, the default, identifies only those PIRA events sustained for the remaining recorded follow-up.

### Value

A data frame.

### References

Dzau, et al. Journal of Neurology, Neurosurgery & Psychiatry 2023;94(12):984-991.

### Examples

```
data(SampleData)
output<-PIRA(SampleData)
```

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SampleData	<i>Expanded disability status scale (EDSS) score and functional system score (FSS) recorded at each visit</i>
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### Description

A long data frame containing 12 variables 'ID', 'dateEDSS', 'EDSS', 'FSpyr', 'FScrbl', 'FSbstem', 'FSsens', 'FSsph', 'FSvis', 'FScreb', 'FSamb', 'daysPostRelapse'.

### Usage

SampleData

### Format

A long data frame with 798 rows and 12 variables:

**ID** (character) patient ID

**dateEDSS** (date YYYY-mm-dd) date of disability score

**EDSS** (numeric) disability score (Expanded Disability Status Scale; EDSS)

**FSpyr** (numeric) pyramidal functional system score

**FScrbl** (numeric) cerebellar functional system score

**FSbstem** (numeric) brainstem functional system score

**FSsens** (numeric) sensory functional system score

**FSsph** (numeric) bowel & bladder functional system score

**FSvis** (numeric) visual functional system score

**FScreb** (numeric) cerebral functional system score

**FSamb** (numeric) ambulation functional system score

**daysPostRelapse** (numeric) days since most recent relapse

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spmsDx

*Identification of secondary progressive multiple sclerosis*

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### Description

Identify conversion from relapsing-remitting multiple sclerosis (RRMS) to secondary progressive multiple sclerosis (SPMS), using the CORE definition, including Functional System Scores (FSS) of Expanded Disability Status Scale (EDSS). The identification of SPMS is based on clinical visit records, each record including entries for patient code, visit date, EDSS score, FSS, ambulation score, and days since most recent relapse. If a baseline EDSS score and corresponding FSS are not provided, these are determined as the first EDSS score and corresponding FSS recorded in the dataset, outside 30 days (the default) of a relapse. Following a relapse, the first EDSS score recorded in the dataset outside 30 days (the default) of a relapse, becomes the new baseline EDSS score. SPMS is sustained for the remainder of the follow-up, unless followed by two consecutive improvements in EDSS scores.

**Usage**

```
spmsDx(
  visits,
  minEDSS = 4,
  minFSpyr = 2,
  tRelapse = 30,
  tProgression = 3 * 30.25,
  tRegression = 9 * 30.25,
  tRelProg = 6 * 30.25
)
```

**Arguments**

<code>visits</code>	A data frame consisting of 22 columns: ID, dateEDSS, EDSS, FSpyr (pyramidal FSS), FScrbl (cerebellar FSS), FSbstem (brainstem FSS), FSsens (sensory FSS), FSsph (bowel bladder FSS), FSvis (visual FSS), FScreb (cerebral FSS), FSamb (ambulation score), dateBlincVisit, bEDSS (baseline EDSS), bFSpyr (baseline pyramidal FSS), bFScrbl (baseline cerebellar FSS), bFSbstem (baseline brainstem FSS), bFSsens (baseline sensory FSS), bFSsph (baseline bowel bladder FSS), bFSvis (baseline visual FSS), bFScreb (baseline cerebral FSS), bFSamb (baseline ambulation score), daysPostRelapse (days since most recent relapse).
<code>minEDSS</code>	Minimum EDSS score required to reach SPMS conversion.
<code>minFSpyr</code>	Minimum pyramidal FSS to reach SPMS conversion.
<code>tRelapse</code>	Minimum time in days since the most recent relapse to EDSS assessment.
<code>tProgression</code>	SPMS confirmation period in days.
<code>tRegression</code>	Confirmation period for EDSS improvement in days.
<code>tRelProg</code>	Confirmation period (days) for re-baselining EDSS (after a relapse led to non-confirmed increase in EDSS).

**Value**

A data frame.

**References**

Lorscheider J, et al. *Brain* 2016; 139 (9): 2395-2405.

**Examples**

```
data(SampleData)
output<-spmsDx(SampleData)
```

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spmsDx_no_fss	<i>Identification of secondary progressive multiple sclerosis without functional system scores and ambulation score</i>
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### Description

Identify conversion from relapsing-remitting multiple sclerosis (RRMS) to secondary progressive multiple sclerosis (SPMS), using the CORE definition without Functional System Scores (FSS) of Expanded Disability Status Scale (EDSS). The identification of SPMS is based on clinical visit records, each record including entries for patient code, visit date, EDSS score, and days since most recent relapse. If a baseline EDSS score is not provided, this is determined as the first EDSS score recorded in the dataset, outside 30 days (the default) of a relapse. Following a relapse, the first EDSS score recorded in the dataset outside 30 days (the default) of a relapse, becomes the new baseline EDSS score. SPMS is sustained for the remainder of the follow-up, unless followed by two consecutive improvements in EDSS scores.

### Usage

```
spmsDx_no_fss(
  visits,
  minEDSS = 4,
  tRelapse = 30,
  tProgression = 3 * 30.25,
  tRegression = 9 * 30.25,
  tRelProg = 6 * 30.25
)
```

### Arguments

visits	A dataframe consisting of 6 columns: ID, dateEDSS, EDSS, dateBlIneVisit, bEDSS (baseline EDSS), daysPostRelapse (days since most recent relapse).
minEDSS	Minimum EDSS score required to reach SPMS conversion.
tRelapse	Minimum time in days since the most recent relapse to EDSS assessment.
tProgression	SPMS confirmation period in days.
tRegression	Confirmation period for EDSS improvement in days.
tRelProg	Confirmation period (days) for re-baselining EDSS (after a relapse led to non-confirmed increase in EDSS).

### Value

A data frame.

### References

Lorscheider J, et al. *Brain* 2016; 139 (9): 2395-2405.  
 Brown JW, et al. *JAMA* 2019; 321 (2): 175-87.  
 Lizak N, et al. *JAMA Neurology* 2020; 77 (11): 1398-407.

**Examples**

```
data(SampleData)  
output<-spmsDx_no_fss(SampleData)
```

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