

Helping to ease the pain with R / RMarkdown

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SATRDAY, Cape Town, 18 February 2017



2 n-grams of journal article titles from *PAIN* (2010 - 2017)

chronic pain neuropathic pain



Difficult to treat



Atypical pain medicines

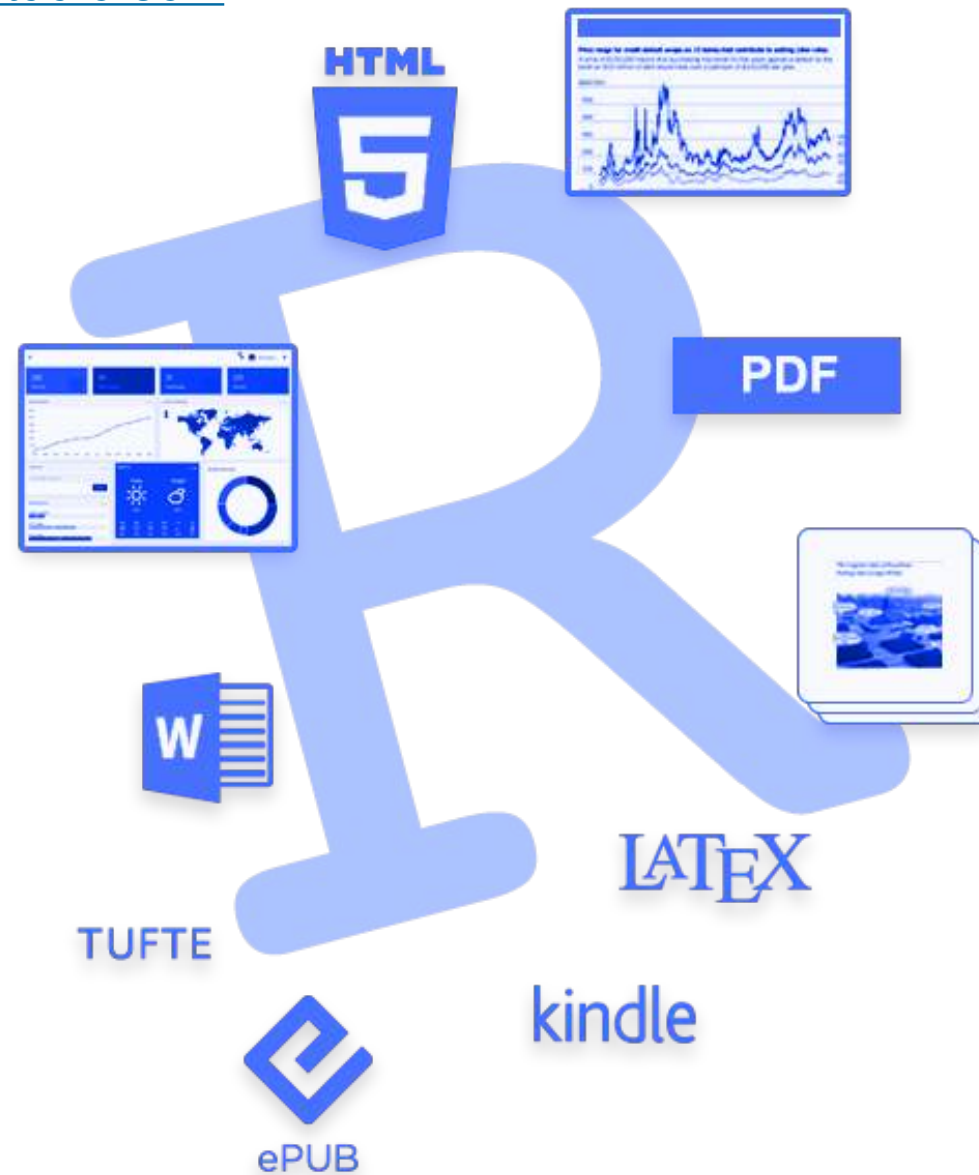
- Anti-depressants
- Anti-convulsants

Goal

**Apply to have medication included on
WHO Essential Medicine List**

RMarkdown

<http://rmarkdown.rstudio.com>



RMarkdown

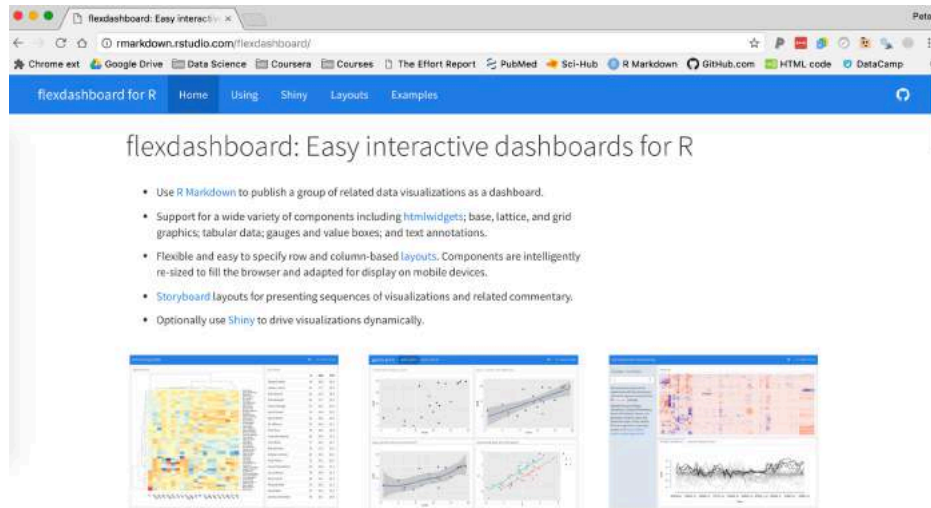
<http://rmarkdown.rstudio.com>

Web content

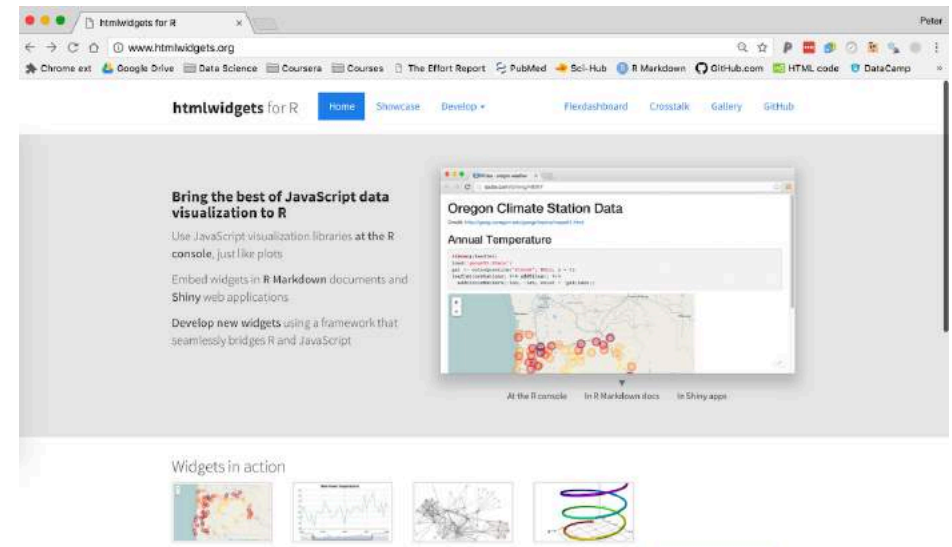


Create a storyboard

Flexdashboard



htmlwidgets



Create a storyboard

Flexdashboard and htmlwidgets

The screenshot shows the RStudio interface with a project titled "neuropathic-pain-storyboard-2016". The main editor displays the R Markdown file "Index.Rmd" with the following content:

```
1 ---
2 title: 'Neuropathic pain: So many people, but where are the drugs?'
3 output:
4   flexdashboard::flex_dashboard:
5     storyboard: true
6     navbar:
7     - { title: 'painblogR.org', icon: 'fa-home', href:
8       'http://painblogr.org/', align: right }
9     social: ['twitter', 'facebook', 'linkedin', 'google-plus']
10    source_code: 'https://github.com/kamermanpr/WHO-EML-storyboard-2016'
11    favicon: 'https://dl.dropboxusercontent.com/u/11805474/painblogr/neuropathic-pain-storyboard-2016/favicon.ico'
12    self_contained: false
13    lib_dir: 'https://dl.dropboxusercontent.com/u/11805474/htmlwidgets'
14  ---
15  {r setup, include = FALSE, warning = FALSE, message = FALSE}
16  library(flexdashboard)
17  library(dplyr)
18  library(tibble)
19  library(tidyr)
20  library(ggplot2)
21  library(ggiraph)
22  library(viridis)
23  library(scales)
24  library(highcharter)
25  library(leaflet)
26  library(sp)
27
28  knitr::opts_chunk$set(cache = FALSE,
29    fig.cap = TRUE,
30    fig.align = 'center')
31
32  ...
```

The right-hand pane shows the "Environment" tab with a file explorer view of the project directory. The files listed are:

Name	Size	Modified
..		
data		
https:		
rscrip		
LICENSE.md	598 B	Sep 3, 2016, 11:38 AM
README.md	3.3 KB	Sep 11, 2016, 10:37 AM
index.html	3.7 MB	Feb 16, 2017, 10:41 PM
.gitignore	74 B	Sep 8, 2016, 10:48 PM
neuropathic-pain-storyboard-20...	277 B	Sep 3, 2016, 12:02 PM
index.Rmd	42.5 KB	Feb 16, 2017, 10:41 PM
Makefile	1024 B	Sep 8, 2016, 10:42 PM

The bottom status bar shows the current line is 1:1, and the text "Neuropathic pain: So many people, but where are the drugs? : R Markdown".

Create a storyboard

Neuropathic pain: So many people, but where are the drugs?

1. **Introduction:** Neuropathic pain is a debilitating form of chronic pain. Learn more about it in this storyboard.
(navigate through the storyboard by clicking on the panels in this top row).

2. **How common is neuropathic pain?** Neuropathic pain is estimated to affect 7 to 10% of adults globally; that's between 518 to 740 million people².

3. **Are we winning the war on neuropathic pain?** No. The burden of neuropathic pain is likely to increase in the future, with developing countries being worst affected.

4. **Why does neuropathic pain matter?** Neuropathic pain has a significant adverse impact on life, health and function; even more so than other causes of chronic pain⁸.

5. **Neuropathic pain: What does it feel like?**

What does neuropathic pain feel like?

Term	Relative Frequency (approximate)
burning	35%
numbness	25%
pins-n-needles	15%
electric shocks	10%
tingling	10%
itching	5%
painful cold	5%

Imagine having a pain that has been described as being 'Worse than death'. A pain that may feel like your *skin is on fire*, and at the same time the painful area may be *numb*. In some cases even the lightest of touches, such as your clothes on your skin, may be excruciatingly painful. **This is what it can feel like to have neuropathic pain.**

This storyboard will introduce you to this unusual type of chronic pain and its treatment.

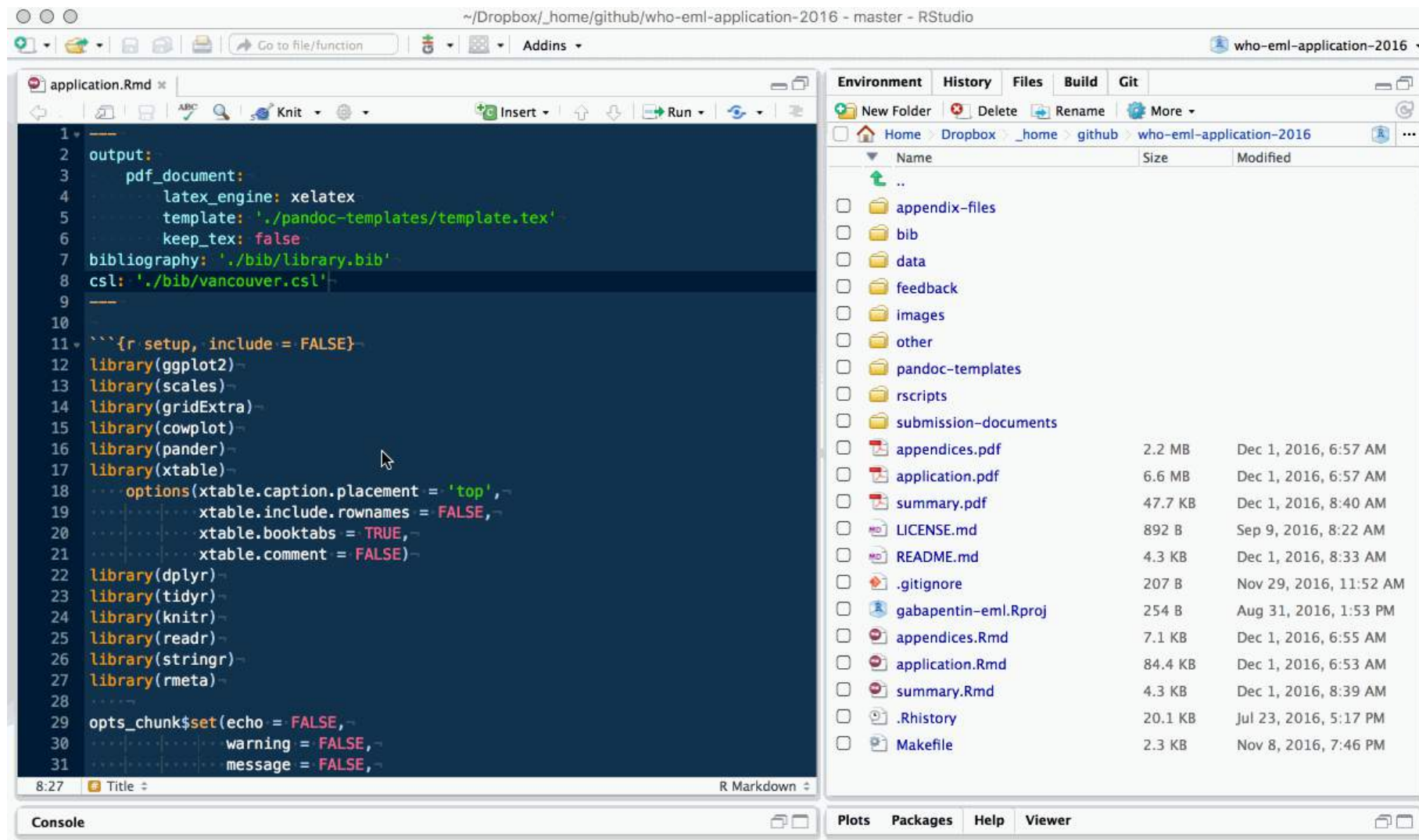
Navigation: Every section of the storyboard consists of an interactive plot on the left (try it out by hovering your mouse arrow over the adjacent plot), and a text panel on the right. The text panel expands on the question stated in the numbered navigation panel above, and provides a legend for the figure. The figure provides illustrative data that complements the text.

Interactive plot: What does neuropathic pain feel like? The plot shows the relative frequency of terms used by 89 individuals with various causes of nervous system injury (e.g., traumatic nerve injury, post-herpetic neuralgia, polyneuropathies, stroke pain; block size is proportional to frequency). 'Burning' was the most commonly used term, but most patients use several terms to describe their pain¹.

Created by: painblogR

painblogr.org/neuropathic-pain-storyboard-2016/

Create a report



The screenshot shows the RStudio interface. The main editor displays an R Markdown file named `application.Rmd`. The file contains YAML front-matter for output, bibliography, and csl, followed by R code for library loading and options setting. The right-hand pane shows the file explorer for the project `who-eml-application-2016`, listing various files and folders.

```
1 ---
2 output:
3   pdf_document:
4     latex_engine: xelatex
5     template: './pandoc-templates/template.tex'
6     keep_tex: false
7 bibliography: './bib/library.bib'
8 csl: './bib/vancouver.csl'
9 ---
10
11 ```{r setup, include = FALSE}
12 library(ggplot2)
13 library(scales)
14 library(gridExtra)
15 library(cowplot)
16 library(pander)
17 library(xtable)
18 options(xtable.caption.placement = 'top',
19         xtable.include.rownames = FALSE,
20         xtable.booktabs = TRUE,
21         xtable.comment = FALSE)
22 library(dplyr)
23 library(tidyr)
24 library(knitr)
25 library(readr)
26 library(stringr)
27 library(rmeta)
28
29 opts_chunk$set(echo = FALSE,
30                warning = FALSE,
31                message = FALSE,
```

Name	Size	Modified
..		
appendix-files		
bib		
data		
feedback		
images		
other		
pandoc-templates		
rscrips		
submission-documents		
appendices.pdf	2.2 MB	Dec 1, 2016, 6:57 AM
application.pdf	6.6 MB	Dec 1, 2016, 6:57 AM
summary.pdf	47.7 KB	Dec 1, 2016, 8:40 AM
LICENSE.md	892 B	Sep 9, 2016, 8:22 AM
README.md	4.3 KB	Dec 1, 2016, 8:33 AM
.gitignore	207 B	Nov 29, 2016, 11:52 AM
gabapentin-eml.Rproj	254 B	Aug 31, 2016, 1:53 PM
appendices.Rmd	7.1 KB	Dec 1, 2016, 6:55 AM
application.Rmd	84.4 KB	Dec 1, 2016, 6:53 AM
summary.Rmd	4.3 KB	Dec 1, 2016, 8:39 AM
.Rhistory	20.1 KB	Jul 23, 2016, 5:17 PM
Makefile	2.3 KB	Nov 8, 2016, 7:46 PM

+ Lots of time on... StackExchange  **TEX**

Create a report

Cover page

Gabapentin for Neuropathic Pain

An application to the 21st meeting of the WHO Expert Committee on Selection and Use of Essential Medicines for the inclusion of gabapentin on the WHO Model List of Essential Medicines

Submitted by
International Association for the Study of Pain (IASP)
Neuropathic Pain Special Interest Group (NeuPSIG) of the IASP
International Association of Hospice and Palliative Care (IAHPC)

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Supporting organizations	5
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Layout

GABAPENTIN FOR NEUROPATHIC PAIN			
	First-line drugs		
	Serotonin-noradrenaline reuptake inhibitors duloxetine and venlafaxine	Tricyclic antidepressants	Pregabalin, gabapentin, gabapentin extended release or enacarbil
Quality of evidence	High	Moderate	High
Balance between desirable and undesirable effects			
Effect size	Moderate	Moderate	Moderate
Tolerability and safety*	Moderate	Low-moderate	Moderate-high
Values and preferences	Low-moderate	Low-moderate	Low-moderate
Cost and resource allocation	Low-moderate	Low	Low-moderate
Strength of recommendation	Strong	Strong	Strong
Neuropathic pain conditions	All	All	All

Figure 8: Summary of the GRADE recommendations by Finnerup et al., 2015 [3] for first-line medications for managing neuropathic pain.

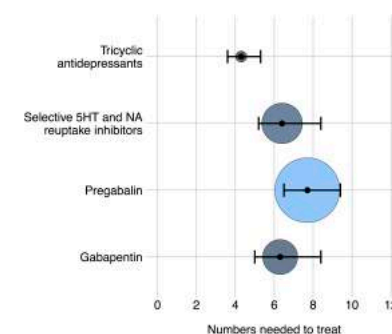


Figure 9: Mean (95% CI) numbers needed to treat (NNT) for first-line medications recommended by Finnerup et al., 2015 [3]. The size of the coloured circles indicate the relative number of individuals randomized in trials for a particular medication. Data from Finnerup et al., 2015 were updated to include two new trials in the tricyclic antidepressant class, and gabapentin extended release and enacarbil were excluded from the gabapentin group.

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www.who.int/selection_medicines/...



Create a report

Layout

Summary of efficacy and safety across first-line medications

Tables 3 summarises the benefits and harms of gabapentin based on our systematic review and meta-analysis. For comparison, we have also included the data for other medicines we recommended as first-line [3] (a more granular summary of the GRADE analysis for gabapentin only is provided in Table 4). Based on the balance of the evidence, we recommended gabapentin, pregabalin, TCAs and SNRIs as first-line treatments; the updated literature search in 2016 did not change our recommendation. When making our original recommendations, we stated that there was no evidence for any of the agents having superior efficacy in general, or for specific causes of neuropathic pain; and nor did the updated search not alter our position on these issues. Therefore, our recommendations applied to neuropathic pain in general. However, we also noted the paucity of clinical trials on cancer-related neuropathic pain, and the absence of trials in children.

Table 3: Summary of efficacy and adverse events reported by Finnerup et al., 2015 [3]

	Number needed to treat (50% / 30% / moderate pain relief)	Number needed to harm			
		Major*	Dizziness	Somnolence	Dry mouth
TCA	4.3	13.4	10.3	9.5	4.8
Gabapentin†	6.3	25.6	5.1	7.1	-
Pregabalin	8.8	13.9	-	-	-
SNRI	6.4	11.8	-	-	-

TCA: Tricyclic antidepressants; SNRI: Serotonin and noradrenaline re-uptake inhibitors;

* : Withdrawal from study because of adverse events;

† : Excluding gabapentin extended release / enacarbil

In their guideline on the management of neuropathic pain, NICE generated a heat-map of relative benefits and harms of the medications they assessed [4]. Figure 16 presents a summary of that figure that only includes medications recommended as first-line therapy by NICE [4] and others [3,5,6].

Summary of available data on comparative cost and cost-effectiveness within the pharmacological class or therapeutic group.

Comparative costs

Comparative pricing data were obtained from the Management Sciences for Health (MSH) International Drug Price Indicator Guide [92]. Tables 5 to 7 report comparative prices of gabapentin and two other medications on the WHO Model Essential Medicines List, amitriptyline and carbamazepine. Amitriptyline was included because it is recommended, along with gabapentin as a first-line pharmacological treatment for neuropathic pain [3–6]. Carbamazepine falls into the same therapeutic class as gabapentin (anticonvulsants), and it is recommended for the treatment of trigeminal neuralgia [6]¹¹. The data are reported as unit price of the medications (Table 5), price when prescribed at the defined daily dose for each

¹¹ In our recent meta-analysis and GRADE analysis [3] there was inconclusive evidence for the use of carbamazepine in the management of neuropathic pains outside of trigeminal neuralgia, and thus carbamazepine was not recommended for use in the pharmacological management of neuropathic pain. Even in the case of trigeminal neuralgia, the data supporting the use of carbamazepine is old and of low quality [6].

Reference list

References

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