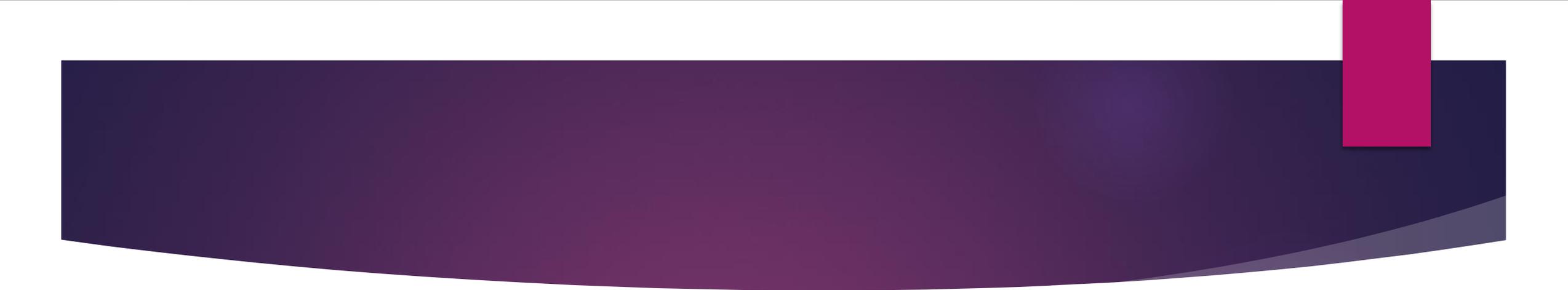


# Do you Treat YES

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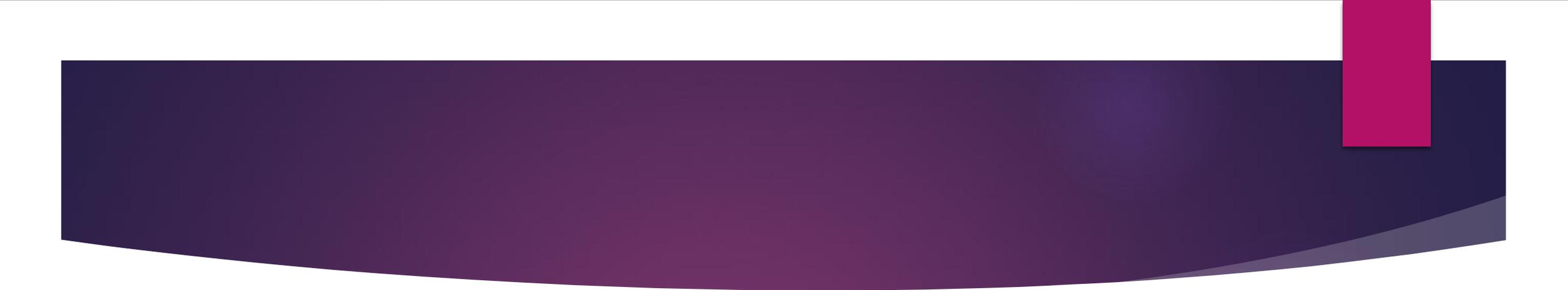
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- ▶ What are the reasons to recommend or perform a treatment
    - ▶ 1- To treat a disease process, including relief of symptoms.
    - ▶ 2- To prevent disease progression.
    - ▶ 3- To prevent major adverse reaction.

So ideally any disease that can be easily and safely treated must be treated.

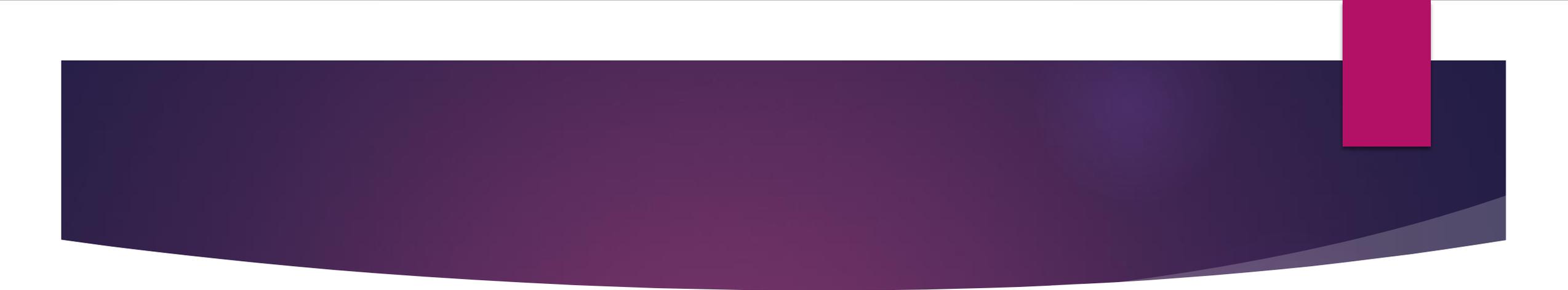
# So in the Brain Aneurysm

- ▶ Do you treat the disease process YES , Actually Maybe, but sometimes No
- ▶ Do we prevent disease progression, YES, actually Maybe but sometimes No
- ▶ Do we prevent adverse reactions from the disease or the treatment, YES, actually Maybe, but sometimes unfortunately NO

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- ▶ So to answer this question there are 2 large studies in the literature.
  - ▶ ISUIA
  - ▶ Japanese Cohort

# Study 1, ISUIA

- ▶ International Study of Unruptured Intracranial Aneurysms (ISUIA) Investigators. Results of the International Study of Unruptured Intracranial Aneurysms. *The Lancet*, July 12, 2003, Vol. 362, No. 9378, pp. 103-110.
- ▶ 4000 patients randomized.
- ▶ Among patients studied, 1,917 had surgery to repair the aneurysm, 451 underwent endovascular coiling, and 1,962 patients did not undergo surgical treatment. Patients were studied for up to 9 years, with an average of 4 to 5 years.



## ▶ Results

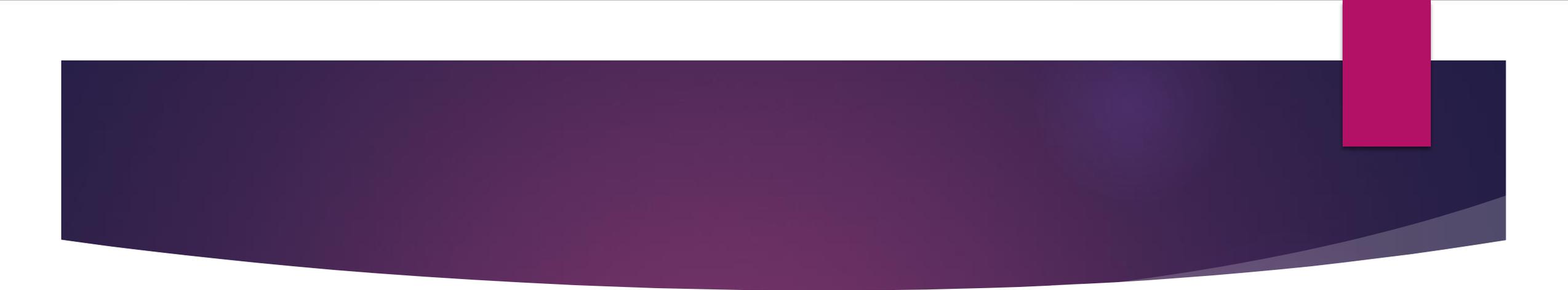
- ▶ Patients with brain aneurysms smaller than 7 millimeters and with no history of a previous hemorrhage were at very low risk of rupture - only about one in a thousand of these aneurysms ruptured each year.
- ▶ Results showed that aneurysm size, location within the brain, and whether the patient has had rupture of a previous aneurysm are significant factors in determining the risk that a newly diagnosed aneurysm will rupture.
- ▶ 7 mm is the cutoff.
- ▶ Posterior circulation is more likely to rupture than anterior circulation

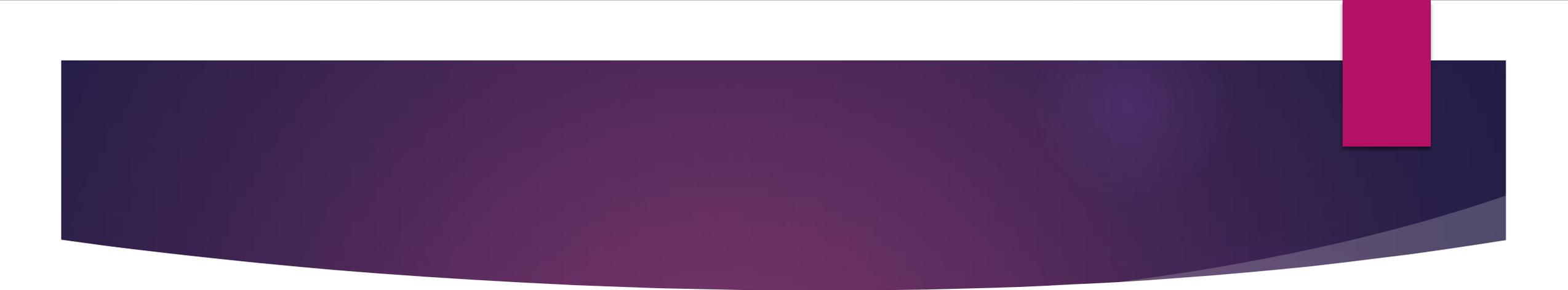
# Japanese Cohort

- ▶ **The Natural Course of Unruptured Cerebral Aneurysms in a Japanese Cohort**
- ▶ The UCAS Japan Investigators
- ▶ N Engl J Med **2012**; 366:2474-2482 [June 28, 2012](#) DOI: 10.1056/NEJMoa1113260
- ▶ 5720 Patients, with 6697 aneurysms.
- ▶ Of the 6697 aneurysms studied, 91% were discovered incidentally. Most aneurysms were in the middle cerebral arteries (36%) and the internal carotid arteries (34%). The mean ( $\pm$ SD) size of the aneurysms was  $5.7 \pm 3.6$  mm.

## ▶ Results

- ▶ With aneurysms that were 3 to 4 mm in size as the reference, the hazard ratios for size categories were as follows: 5 to 6 mm, 1.13 (95% CI, 0.58 to 2.22); 7 to 9 mm, 3.35 (95% CI, 1.87 to 6.00); 10 to 24 mm, 9.09 (95% CI, 5.25 to 15.74); and 25 mm or larger, 76.26 (95% CI, 32.76 to 177.54).
- ▶ As compared with aneurysms in the middle cerebral arteries, those in the posterior and anterior communicating arteries were more likely to rupture (hazard ratio, 1.90 [95% CI, 1.12 to 3.21] and 2.02 [95% CI, 1.13 to 3.58], respectively).
- ▶ Aneurysms with a daughter sac (an irregular protrusion of the wall of the aneurysm) were also more likely to rupture (hazard ratio, 1.63; 95% CI, 1.08 to 2.48).
- ▶ The aneurysms most prone to rupture are located in the anterior communicating and posterior communicating arteries.
- ▶ A history of subarachnoid hemorrhage, former or current smoking, the presence of multiple aneurysms, and hypertension, each of which was identified as an independent risk factor for rupture in other studies,<sup>8,13,14</sup> did not significantly affect the risk of rupture in our cohort.

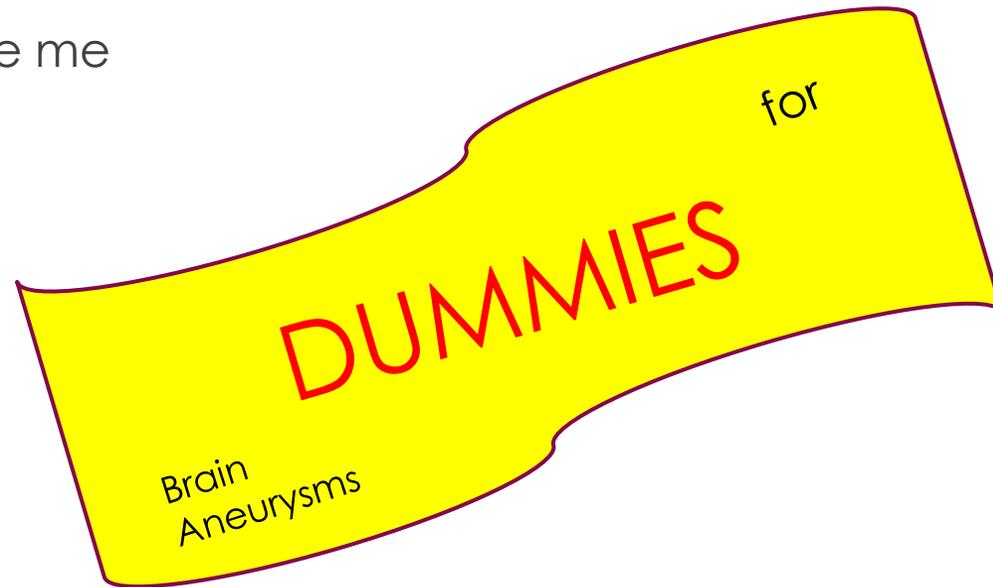
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- ▶ What is interesting is that the 2 large studies of ISUIA and the Japanese cohort study only looked at size and the relationship with rupture.
  - ▶ What is interesting in the Japanese study, is that the investigators did feel comfortable in truly randomizing aneurysms that had morphological criteria that are considered higher risk. Therefore they treated about 2000 patients within the first 4-6 weeks of diagnosis.
  - ▶ None of the studies examined any additional evaluation of the wall pathology or any other imaging findings that could influence the risk of rupture in seemingly low risk patients based on aneurysm size. This is obviously due to lack of clinically proven data in this regards and imaging capabilities to examine such aneurysm wall disease.

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- ▶ Problems with brain aneurysm treatment is that it is very invasive, and carries relatively high risk. So before recommending treatment we need to establish a benefit for the treatment more than the risk of the natural history of the disease.
  - ▶ The problem is that the natural history of the disease is very variable and extremely unpredictable.
  - ▶ Elegant studies with major efforts with thousands of patients being followed for several years have been performed. The results of those studies are published yet sorry to say that those results do not frequently mirror our practice. In my opinion the studies have a placebo effect on the physicians. In addition it is putting the burden of proof on the patient.

# What Does the Patient Hear

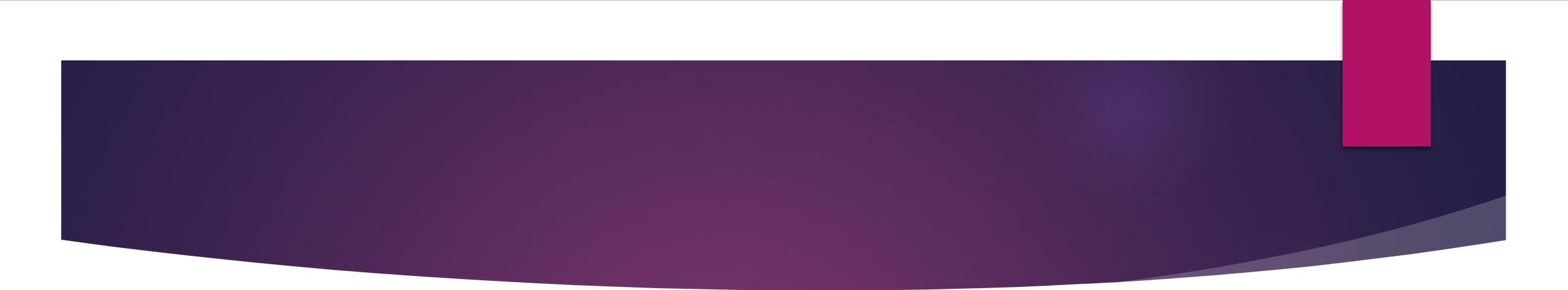
- ▶ The patient has to deal with knowing that they have a “potentially life-threatening” disease, yet we are not sure if we should do anything about it. BUT IT IS NOT A TICKING BOMB WAITING TO EXPLODE.
- ▶ Your risk is maybe 1-2 % per year. What does that mean
- ▶ If you rupture you have a 40-50 % chance of death within the first 2 months.
- ▶ If you have symptoms like headache, you will likely not get better.
- ▶ If you do not bleed your chances for next year will be more than this year.
- ▶ If you have a change in the size over time, then your risk will probably increase.
- ▶ You have to decide after “all this information”
  - ▶ OK DOCTOR KILL ME NOW PLEASE

- ▶ Then to look smart in front of our colleagues and the world we make debates about it.
- ▶ So please give me



# In Summery

- ▶ In my personal opinion our problem is that we are invasive in our treatment and we do cause serious complications.
- ▶ If we have a very safe and truly minimally invasive or better yet non invasive way of treating the aneurysm, I believe we should treat them.
- ▶ For now there are a lot of new concepts in endovascular techniques that can potentially be truly minimally invasive such as flow diverters, that will treat the parent artery which is the disease site, rather than the secondary aneurysm sac. The continued development and fine tuning the antiplatelets regime and better yet the newer materials that do not need any antiplatelets can potentially be a great treatment option.
- ▶ We started using flow diverters only to treat extremely difficult and challenging aneurysms, yet I believe they will be better suited for simple small one.

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- ▶ So let's improve our endovascular and open surgical techniques, and I'm sure in due time we will be very confident to always TREAT

THANK YOU