

Société Belge d'Infectiologie et de
Microbiologie clinique

6 november 2008

Prophylaxis of Bacterial Endocarditis Revisited

C. Leport, X. Duval, N. Danchin.
Paris 7 - Paris 5 Universities, France.

Prophylaxis of IE : 1950-2008

- IE persistent MORBIDITY \longrightarrow 50 % pts surgery required
- IE persistent MORTALITY : \approx 20% pts
- Recommendations regularly updated



2007 AHA revision : Prophylaxis only for dental procedure, in pts with the highest risk **from** IE (incidence and outcome)

ANTIBIOTIC PROPHYLAXIS for IE

International Society Chemotherapy working group
PROPOSITIONS : FLEXIBLE PRESENTATION

MINIMAL

versus

MAXIMAL REGIMEN

DENTAL
(upper respir.tract)

GI - UROLOGIC

SINGLE PROC.

MULTIPLE PROC.

CARDIAC RISK

HIGH CARDIAC RISK

OUT PATIENT

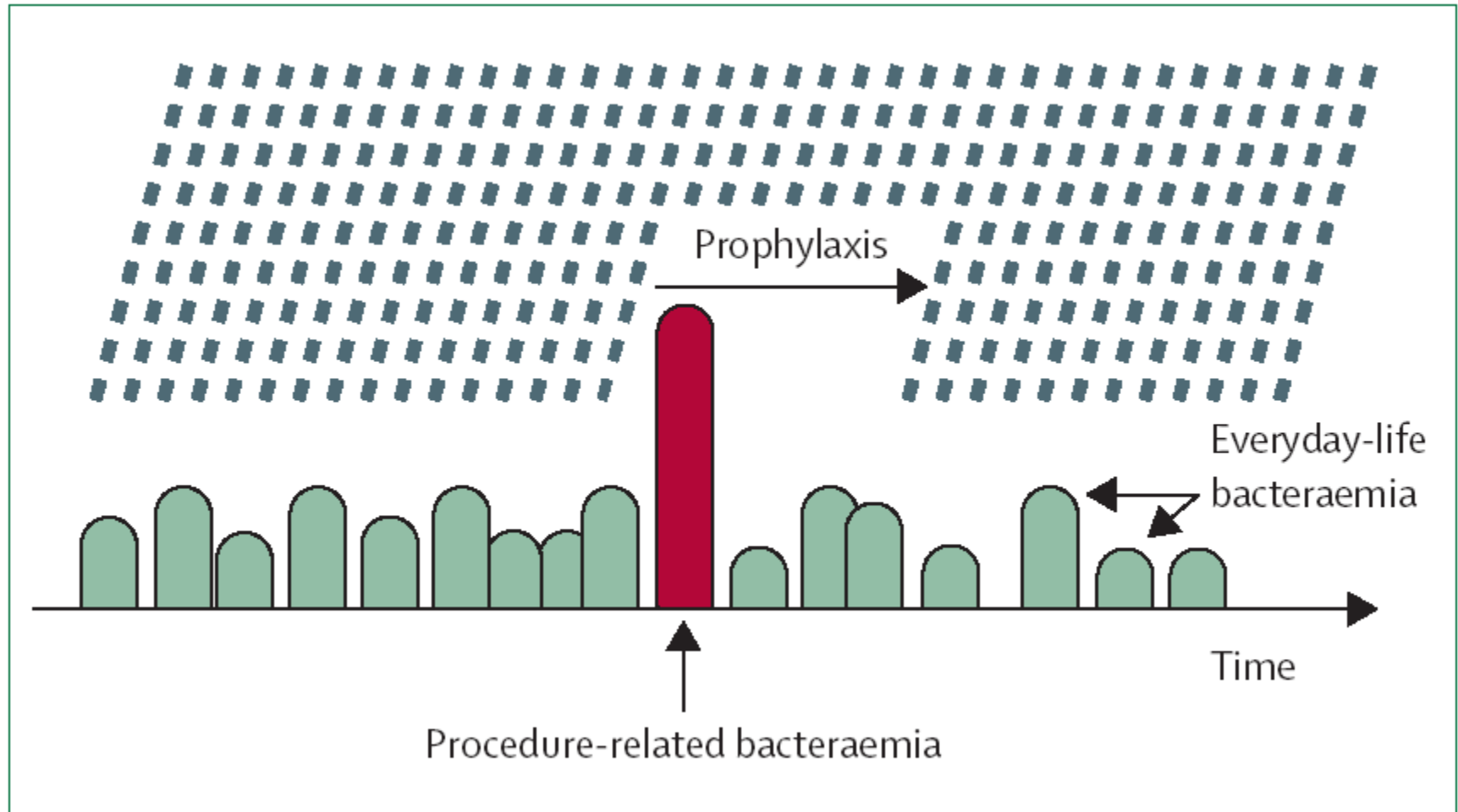
IN PATIENT-
GENERAL ANESTHESIA

Swiss recommendations – 2000

P. Moreillon

1. Switzerland is **not very original** (at least for IE prophylaxis)
2. Clinical and animal studies indicate that IE is related to **spontaneous bacteremia**
3. **Only selected high-risk patients** are likely to benefit from prophylaxis
4. **Single dose oral amoxicillin (2-3 g)** is likely to be appropriate for prophylaxis against peni. R streptococci
5. Single dose oral amoxicillin is very effective against (amoxi-S) Van-S and Van-R *E. faecalis*
6. Single-dose oral amoxicillin should be proposed for high-risk patients undergoing UTI or lower GI tract procedures

Limited role of antibiotic prophylaxis against everyday versus procedure-related bacteriemia



Duval X & Leport C. Lancet Infectious Diseases 2008

France : Recommandations 2002

- To **IMPROVE** general **oral hygiene** and **education**
- To **MAINTAIN** the **PRINCIPLE** of antibiotic prophylaxis after **at risk procedures** in patients with **at risk cardiac conditions**

BUT

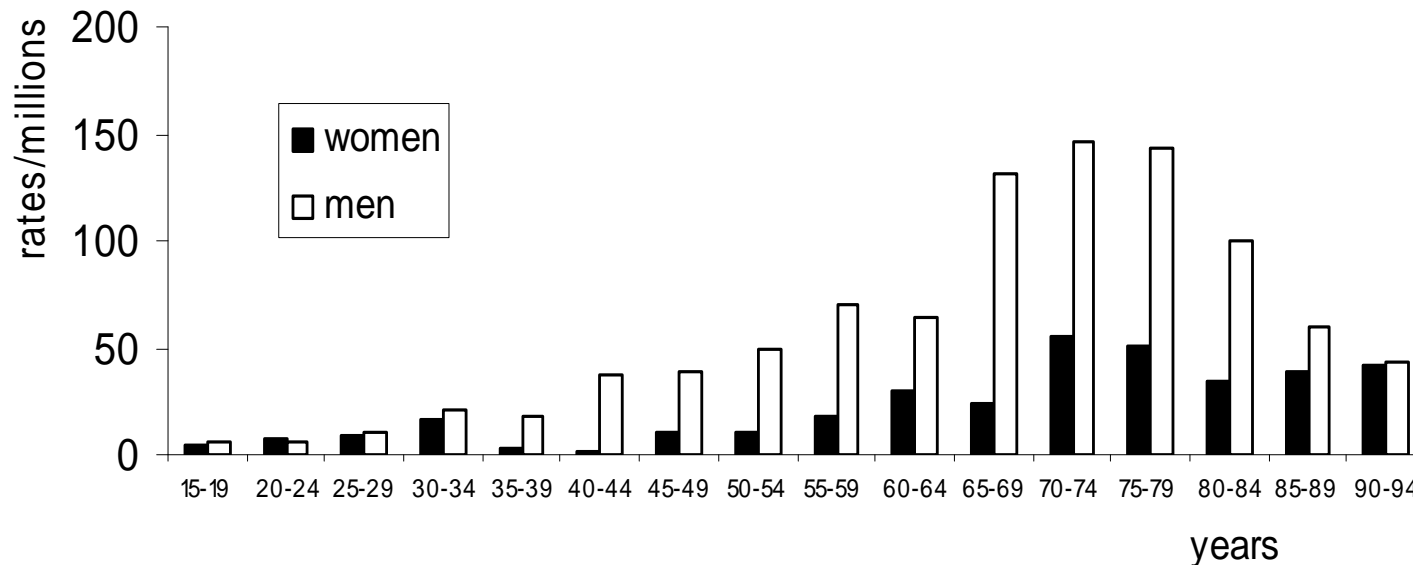
- **REDUCE** the **INDICATIONS** to situations where the **individual benefit** versus **individual and collective risk ratio** is the highest

Changing Profile of Infective Endocarditis -1999

Results of a One-Year Survey in France

French Study Group on Infective Endocarditis

- **390** cases ; 277 M / 113 F - age 59 yrs, [16-95]
- 30 cases / year / million inhabitants (age- and sex- standardized incidence)



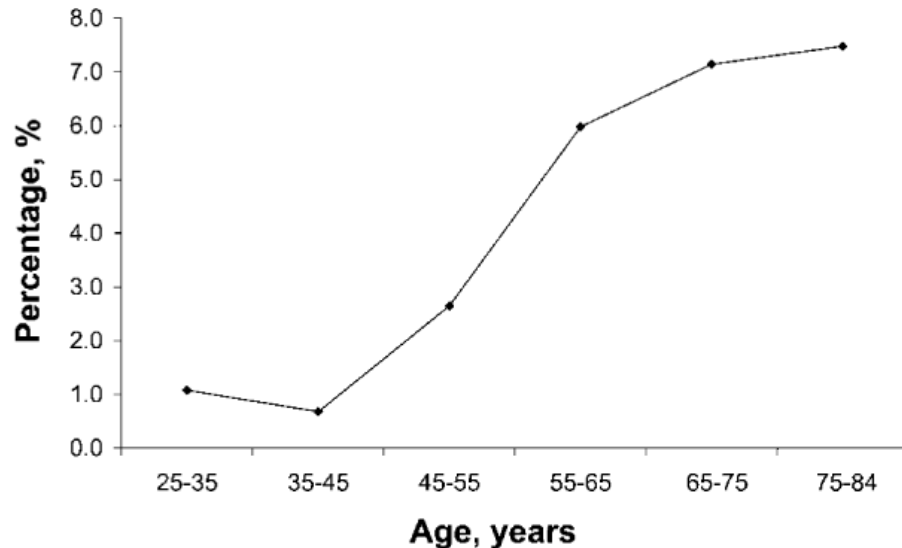
IE one-year French surveys : 1991 vs. 1999

| Incidence (CI 95%) | 1991 | 1999 | P |
|---------------------------------|-------------------------|-------------------------|-------------------|
| Overall standardized | 30.9 [27.9-34.1] | 26.5 [23.9-29.6] | <0.001 |
| Standardized by UHD* | | | |
| - previously known UHD* | 20.6 [18.2-23.4] | 15.1 [13.1-17.5] | <10 ⁻⁸ |
| - prosthetic valve | 6.9 [5.5-8.6] | 4.7 [3.6-6.2] | <0.001 |
| Standardized by pathogen | | | |
| - oral streptococci | 7.8 [6.4-9.5] | 5.1 [4.0-6.7] | <0.001 |
| - group D streptococci | 5.3 [4.1-6.9] | 6.2 [5.0-7.9] | 0.67 |

* UHD : underlying heart disease

Estimated Risk of Endocarditis in Adults with Predisposing Cardiac Conditions Undergoing Dental Procedures With or Without Antibiotic Prophylaxis

Xavier Duval,¹ F. Alla,² B. Hoen,³ F. Danielou,² S. Larrieu,⁴ F. Delahaye,⁵ C. Leport,¹ and S. Briançon²



⇒ 3.3% French population



⇒ Predisposing cardiac condition

Figure 1. Age-specific prevalence of a predisposing cardiac condition among French adults (age, 25–84 years).

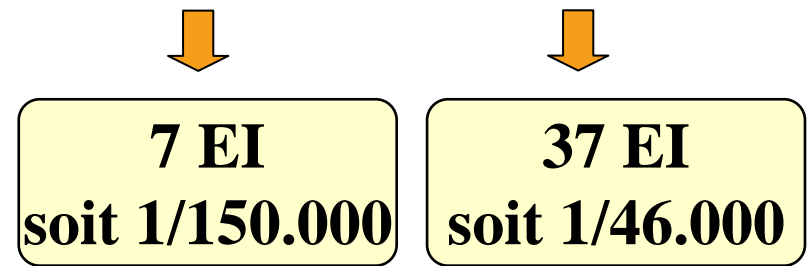
2805 pts Paquid and Canevas cohorts

Table 1. Estimated number of known predisposing cardiac conditions (PCCs) among French adults (age, 25–84 years) and of annual at-risk dental procedures among subjects with PCCs.

| Characteristic | Adults | At-risk dental procedures per year | | |
|--|-------------------|------------------------------------|-----------------------------------|-------------------------------------|
| | | Total | Protected procedures ^a | Unprotected procedures ^b |
| Total | | | | |
| No. (%) of patients or yearly procedures | 1,287,296 | 2,746,384 | 1,042,189 (38) | 1,704,195 (62) |
| 95% CI | 999,196–1,575,396 | 2,304,094–3,188,674 | 748,978–1,335,399 | 1,373,064–2,035,327 |

^a Protected procedures were defined as invasive procedures in which antibiotic prophylaxis was administered.

^b Unprotected procedures were defined as invasive procedure in which antibiotic prophylaxis was not administered.



Risk of IE in at-risk cardiac pts

after at-risk dental procedures

≈ 30 - 40 IE /year in France (2.4%)

POPULATION-based STUDIES (France 2003)

900 000 at-risk dental procedures performed per year, on at-risk pts, without prophylaxis

Risk of IE after at-risk procedures

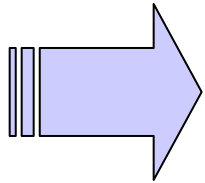
1 /50 000 in pts with native valvulopathy

1 /10 000 in pts with prosthetic valve

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Xavier Duval,¹ F. Alla,² B. Hoen,³ F. Danielou,² S. Larrieu,⁴ F. Delahaye,⁵ C. Leport,¹ and S. Briançon²
Clinical Infectious Diseases 2006;42:e102–7

Results. After standardization, extrapolation of results to the age-equivalent general population (39 millions subjects) indicated the following: first, 3.3% (95% confidence interval [CI], 2.6%–4%) of the subjects had PCC, 2.7 million (95% CI, 2.3–3.2 million) of whom had undergone at least 1 at-risk dental procedures within the survey year, and the procedures were unprotected in 62% of cases; second, 37 (95% CI, 18–68; 2.7%) of the 1370 annual IE cases in France were possibly related to unprotected procedures. Thus, the risks of developing IE were estimated to be 1 in 46,000 for unprotected procedures (1 in 10,700 and 1 in 54,300 for subjects with prosthetic and native valve PCC, respectively) and 1 in 150,000 for protected procedures.



At most 1 /10 700 at-risk procedures (in PV pts) could be responsible for ONE IE

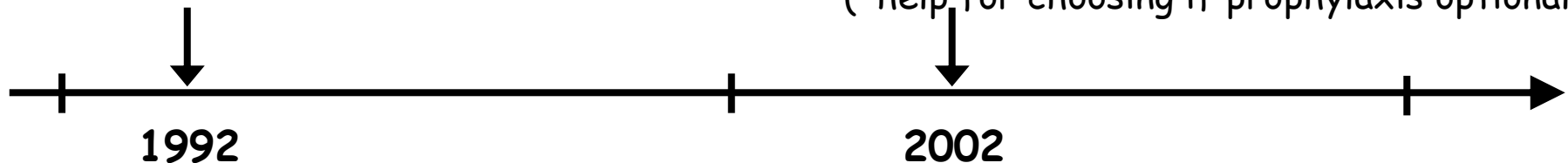
Evolution of French recommendations 2002

When : one hour before an **at risk procedure**

For Whom: pts with **at risk cardiac conditions...**
and other **non cardiac risk factors**

| | 1992 | 2002 |
|-------------------|--|---|
| Procedures | <ul style="list-style-type: none"> -All dental -Almost all extradental | <ul style="list-style-type: none"> - Invasive oral or dental - Extradental procedures: list |
| Patients | <ul style="list-style-type: none"> -Prosthetic cardiac valves -Cyanotic congenital cardiopathies (except IAC) -History of IE -Valvulopathies (AI, MI, AS) -Mitral prolapsus with regurgitation -Bicuspid aortic valve -Obstructive cardiomyopathy | <p>1/ CARDIAC CONDITIONS</p> <ul style="list-style-type: none"> (*) high risk group (**) lower risk group <p>2/ HOST FACTORS*</p> <ul style="list-style-type: none"> -Visceral deficiencies -Diabetes mellitus -Age > 65 years -Immunodepression |

(*help for choosing if prophylaxis optional)



ANTIBIO-PROPHYLAXIE EI

France 2002

Groupe A :

Cardiopathie à **HAUT RISQUE**

RECOMMANDÉE

**Gestes bucco-
dentaires à
risque**


Groupe B :

Cardiop. à **RISQUE MOINS élevé**

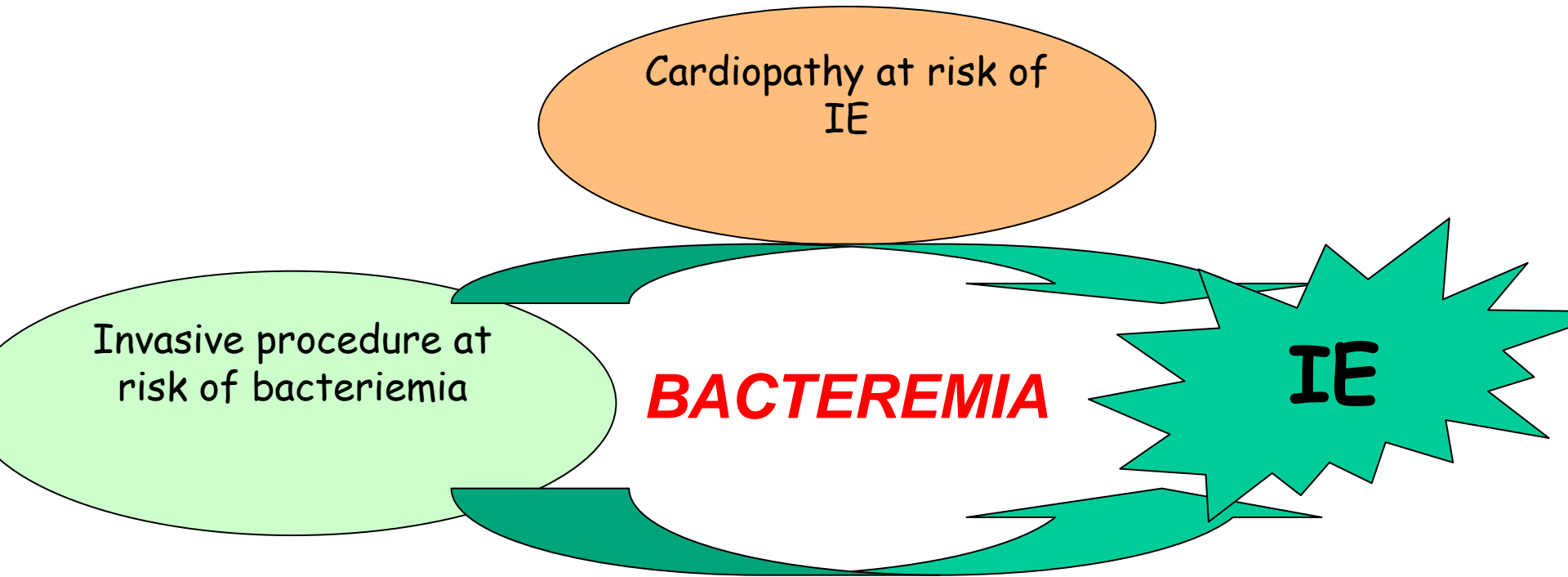
OPTIONNELLE

Gestes bucco-dentaires non à risque : NON recommandée

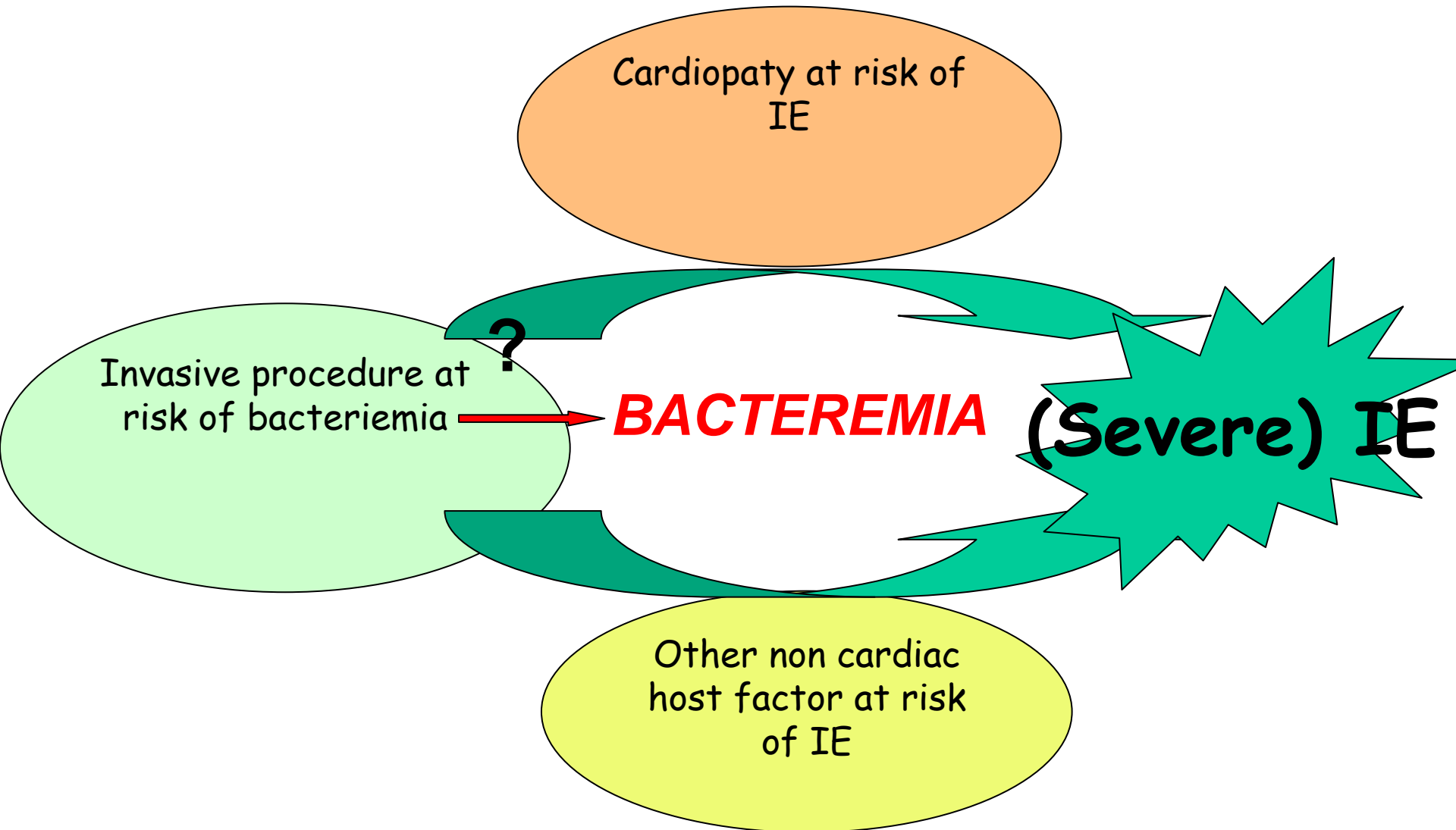
Arguments for the **OPTIONAL** prescription

- **Age > 65 years**
- **Associated conditions**
 - Cardiac, renal, respiratory, hepatic insufficiency
 - Diabetes mellitus
 - Acquired, constitutional or therapeutic ID
- **Oral or dental condition**
 - Especially inadequate oral or dental hygiene
- **Procedure**
 - Heavy bleeding (intensity duration)
 - Technically difficult procedure (prolonged ...)
-  AB may be initiated within the hour following the procedure
- **Patient's informed opinion**

Rational for IE prophylaxis : 1950 -2002



Rational for IE prophylaxis 2002 →



AHA : IE prophylaxis Workshop

May 2004

- Poor compliance with recommendations
- Poor understanding of reco.
- Portal of entry usually unknown
- Known underlying conditions associated with IE
- Some dental procedures cause bacteremia
- Low number of preventable cases
- High morbidity and mortality of IE

Guidelines for the prevention of endocarditis: report of the Working Party of the British Society for Antimicrobial Chemotherapy

F. K. Gould^{1*}, T. S. J. Elliott², J. Foweraker³, M. Fulford⁴, J. D. Perry¹, G. J. Roberts⁵,
J. A. T. Sandoe⁶ and R. W. Watkin⁷

¹*Department of Microbiology, Freeman Hospital, Newcastle upon Tyne, UK;* ²*Department of Microbiology, Queen*

Elizabeth Hospital, Birmingham, UK; ³*Department of Microbiology, Papworth Hospital, Cambridge, UK;*

⁴*Postgraduate Dental Department, University of Bristol, Bristol, UK;* ⁵*King's College Dental Institute, London, UK;*

⁶*Department of Medical Microbiology, Leeds Teaching Hospitals NHS Trust, Leeds, UK;* ⁷*Department of Cardiology, Queen Elizabeth Hospital, Birmingham, UK*

High-risk cardiac factors requiring antibiotic prophylaxis

Previous infective endocarditis

Cardiac valve replacement surgery, i.e. mechanical or biological prosthetic valves

Surgically constructed systemic or pulmonary shunt or conduit

Dental procedures requiring antibiotic prophylaxis

All dental procedures involving dento-gingival manipulation

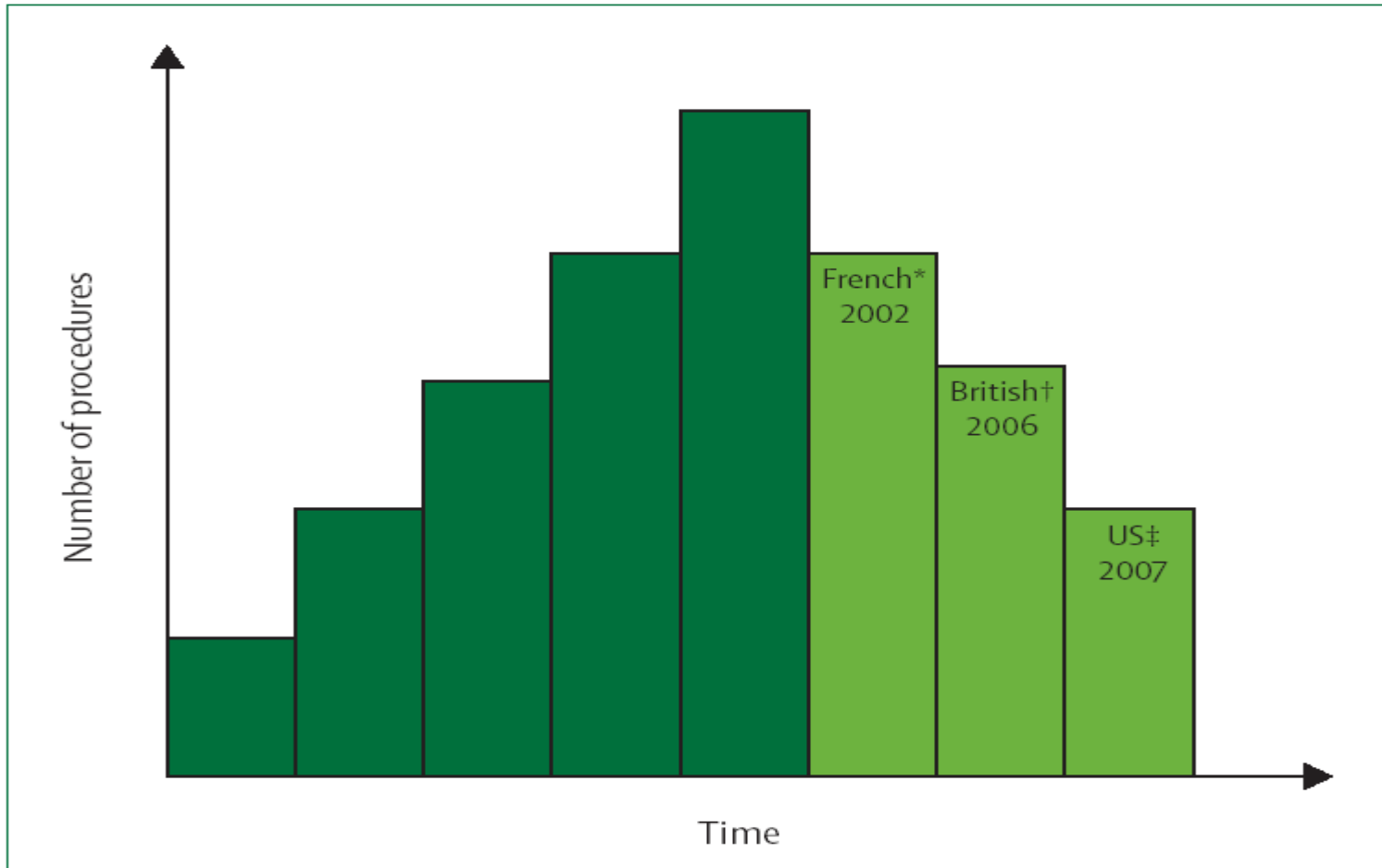
BSAC guidelines 2006

| Procedures | Anecdotaly associated with endocarditis? | % Bacteraemia | Requires IE prophylaxis? |
|-------------------------------------|--|---------------------------|--------------------------|
| Oesophageal varices–sclerotherapy | yes ^{21,22} | 10–50 ^{23,24} | yes |
| Oesophageal stricture dilatation | yes ²⁵ | 21–54 ^{23,26–29} | yes |
| Oesophageal varices–Banding | no | 6 ²³ | no* |
| Oesophageal laser therapy | no | 35 ²³ | yes |
| Endoscopy–upper | yes ^{30–33} | 4 ²³ | no* |
| Sigmoidoscopy/colonoscopy | yes ^{34–37} | 0–9 ^{23,26,38} | no* |
| ERCP | no ³⁹ | 6–11 ²³ | yes |
| Percutaneous endoscopic gastrostomy | no | 0 ⁴⁰ | no* |
| Echocardiography–transoesophageal | yes ⁴¹ | 1–13 ^{42,43} | no* |

Recent Evolution of guidelines



Time to Scale Back (Durack, 1992)



Comparison of recent guidelines that have reduced indications for prophylaxis of IE

Dental procedures

| | Indication for Prophylaxis | |
|---|----------------------------|------------------------|
| | High cardiac risk* | Moderate cardiac risk* |
| French 2002 List of dental procedures | Recommended | Optional |
| BSAC 2006 "all dental procedures with dento-gingival manipulation or endodontics" | Recommended | Abandonned |
| AHA 2007 "Any dental procedure with manipulation of the oral mucosa" | Recommended | Abandonned |

Comparison of recent guidelines that have reduced indications for prophylaxis of IE

Extra dental procedures

| | Indications for prophylaxis | |
|--|-------------------------------|----------------------------------|
| | High cardiac risk* | Moderate cardiac risk* |
| French 2002 List of procedures | Recommended or optional ** | Optional or not recommended** |
| BSAC 2006 List of procedures | Recommended | Recommended |
| AHA 2007 | Abandoned* | Abandoned |

*
Except respiratory and skin procedures

A 44-year old woman

- Asymptomatic Barlow's disease
(mitral regurgitation)
- Diabetes mellitus
 - Retinopathy, nephropathy ;Biguanids, insulin
- Inadequate dental hygiene, previous dental extractions with antibioprophyllaxis

→ Needs tooth's extraction

⇒ **Antibioprophyllaxis ?**

US ?

UK ?

France ?

IE antibioprophyllaxis

COST- EFFECTIVENESS approach

ADVERSE EVENTS (AHA 2007)

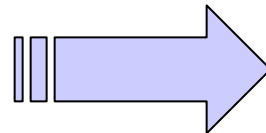
- **Non severe** (rash, diarrhea, gastro-intestinal upset) : common but usually not severe and self limited (single dose) / documented *Clostridium difficile* colitis after a single dose of prophylactic clindamycin : 1 case report
- **Fatal anaphylactic reactions** :
 - Single dose of penicillin : 15 to 25 / 10^6 pts,
1-3 deaths/ 10^6
 - Single dose of cephalosporin : 1 / 10^6 pts
 - Single dose of macrolid or clindamycin :
« extremely rare ». Clarithromycin : cost-effective ?

Resistance of viridans streptococci IE french surveys

- **Oral streptococci**

- R erythromycin

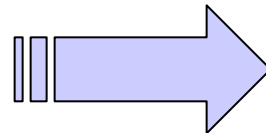
2%, 1991



21% ,1999

- R penicillin

5%, 1991



11%, 1999

- **Gastro-intestinal streptococci**

- 80% R erythromycin; 35% R pristinamycin

STRATEGY for IE prophylaxis – Summary 2007

General consensus on principle for prophylaxis:

FOCUS on HIGHEST RISK situations

☞ **Consensus:**

high cardiac risk – invasive dental procedures

☞ **Debate in other situations :**

moderate cardiac risk ; extra-dental procedures ;

other predisposing host factors

Monitoring IE profile

Cost-effectiveness modelizations

Practitioners and patients feed back

STRATEGY for IE prophylaxis – Summary 2007

CONSIDER GLOBAL APPROACH

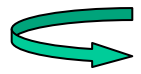
- **Better identification of at risk cardiac pts:**

IE prophylaxis card,

echocardiography report specifying the at-risk cardiac group

General hygiene measures

including oral, dental, skin... (education)



reduce the risk of bacteremia (spontaneous or procedure-related)

- **Discourage some procedures : limit invasive care**

- Propose **systematic twice yearly dental appointment**

SPILF
FFC / SFC
ADF

PRÉVENTION DE L'ENDOCARDITE INFECTIEUSE

Recommandations 2002

Nom, Prénom : _____

Cardiopathie à risque modéré d'endocardite infectieuse (EI) (groupe B) :

- IA, IM, RA, bicuspidie A
- PVM avec IM / épaissement
- Cardiopathie congénitale non cyanogène
- CMH obstructive

Remis par le Dr. : _____ le : _____

à : _____ tel : _____

www.infectiologie.com www.sfcardo.com www.fedecardo.com

www.adf.asso.fr; AEPEI Hôp.Bichat-Claude Bernard - 75877 Paris Cedex 18

SPILF
FFC / SFC
ADF

PRÉVENTION DE L'ENDOCARDITE INFECTIEUSE

Recommandations 2002

Nom, Prénom : _____

Cardiopathie à risque élevé d'endocardite infectieuse (EI) (groupe A) :

- Prothèse valvulaire
- Antécédent d'EI
- Cardiopathie congénitale cyanogène

Remis par le Dr. : _____ le : _____

à : _____ tel : _____

www.infectiologie.com www.sfcardo.com www.fedecardo.com

www.adf.asso.fr; AEPEI Hôp.Bichat-Claude Bernard - 75877 Paris Cedex 18

Cette carte doit être systématiquement montrée à votre médecin / votre dentiste
En cas de soin dentaire à risque, traitement antibiotique préventif facultatif, à discuter avec eux

Si décision de traitement antibiotique préventif
Prendre en une seule prise, par la bouche, dans l'heure précédente
Si pas d'allergie connue aux β -lactamines : Amoxicilline : 3 g
(si poids < 60 kg : 2g - enfant : 75 mg/kg)
Si allergie connue aux β -lactamines : Pristinamycine : 1g (enfant : 25mg/kg),
ou Clindamycine : 600 mg (enfant : 25mg/kg)

Dans tous les cas, en cas de fièvre (en particulier dans les semaines suivant un soin dentaire):

- prévenir votre médecin
- lui présenter cette carte
- ne pas prendre d'antibiotiques sans son avis

Cette carte doit être systématiquement montrée à votre médecin / votre dentiste
En cas de soin dentaire à risque, traitement antibiotique préventif impératif

Prendre une seule prise, par la bouche, dans l'heure précédente
Si pas d'allergie connue aux β -lactamines : Amoxicilline : 3 g
(si poids < 60 kg : 2g - enfant : 75 mg/kg)
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- lui présenter cette carte
- ne pas prendre d'antibiotiques sans son avis

PREVENTION OF BACTERIAL ENDOCARDITIS

Wallet Card

This wallet card is to be given to patients (or parents) by their physician. Healthcare professionals: Please see back of card for reference to the complete statement.

Name: _____

needs protection from **BACTERIAL ENDOCARDITIS**
because of an existing heart condition.

Diagnosis: _____

Prescribed by: _____

Date: _____

Healthcare Professionals – Please refer to these recommendations for more complete information as to which patients and which procedures need prophylaxis.



The Council on Scientific Affairs of the American Dental Association has approved this statement as it relates to dentistry.

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American Heart Association | American Stroke Association

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Dallas, Texas 75231-4596
americanheart.org

50-1605 0705

ANTIBIOTIC PROPHYLAXIS for IE

PATIENTS' EDUCATION

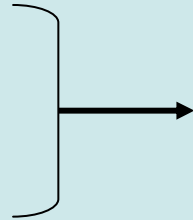
In any case,

Visit your GP in case of **FEVER after a procedure,
with or without AB prophylaxis**

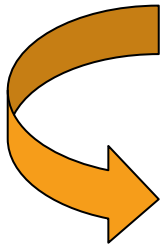
****BLOOD CULTURES before** starting any **ANTIBIOTIC****

Evolution in the strategies for IE prophylaxis : where do we go ? (ECCMID, april 2008)

Valvular diseases
At risk procedures



Antibiotics for
Streptococcus sp. IE



2002 – 2007

- Other risk factors ?
(diabetes...)
- Other bacteria ?
(staphylococci)

Other prophylactic
means ?

Prophylaxis against infective endocarditis

Implementing NICE guidance

2008

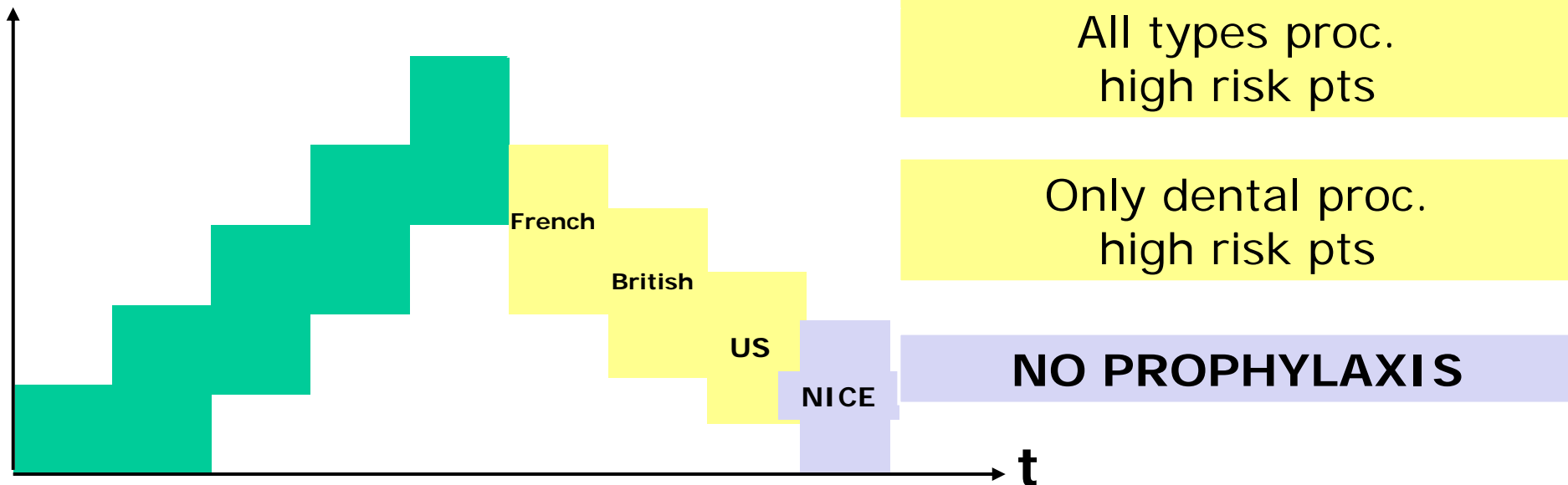
NICE clinical guideline 64



IE Prophylaxis - 2008

Expert guidelines & consensus

- USA (AHA): 1954, 1965, 1977, 1984, 1990, 1997, 2007
- GB (BSAC): 1982, 1986, 1990, 1992, 2006
- Suisse : 1984, 2000
- ESC : 2004
- France : 1992, 2002



Danchin. *Heart* 2005/ Gould. *JAC* 2006 / Wilson. *Circulation* 2007 / X. Duval *Lancet Infect Dis* 2008 / X. Duval *Heart* 2008

NICE : How this guidance changes practice ?

Antibiotic prophylaxis has not been proven to be effective
and
there is no clear association between episodes of IE and
interventional procedures.

We recommend that antibiotic prophylaxis is no longer
offered routinely
for the interventional procedures listed in this guideline

Decisions for your patient

A case-based approach : 76-year old man

- Calcified aortic stenosis
- Diabetes mellitus ; Sulfamides
- Facial cellulitis 6 months ago; successful outcome with oral pristinamycin
- Basal cell carcinoma of the nasal wing

→ Needs a surgical resection

⇒ **Antibioprophylaxis ?**

US ?

UK ?

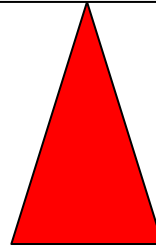
France ?

Prophylaxis of IE - 2008

the **JUST MESSAGE** ?

SIMPLE
CONSENSUAL
for
EFFICIENCY

CLEAR
PROGRESSIVE
for
ACCEPTABILITY



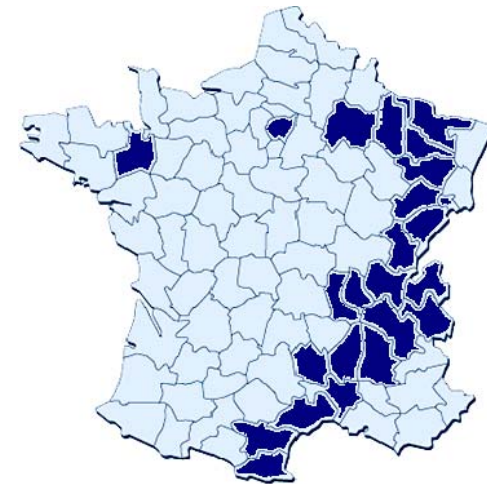
👉 **IMPACT of CHANGES to be EVALUATED**



EI 2008

Régions concernées :

Franche-Comté, Ile et Vilaine, Languedoc-Roussillon, Lorraine, Marne, Paris et Petite couronne, Rhône-Alpes.



Signalements : 1^{er} décembre 2007 - 30 mars 2009

Protocole et renseignements pratiques sur www.endocardite.fr