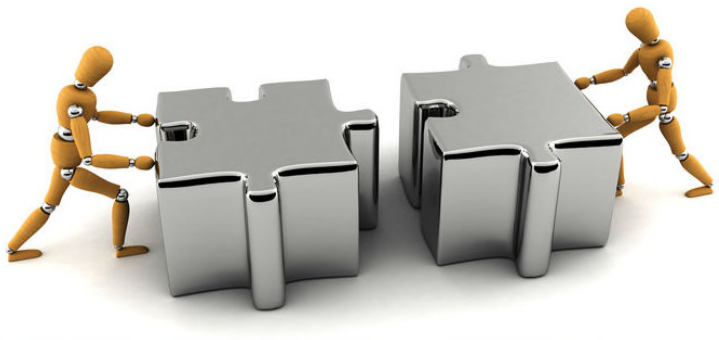
歐盟醫療器材法規(MDR)訓練課程
臨床評估與文獻檢索暨計畫與評估報告實作

- **Wendell Chang**
- 張日聖

- 20210514

臨床評估
(Article 61, Annex XIV)



Definition of Clinical Evaluation

- “clinical evaluation” means a systematic and planned process to continuously generate, collect, analyses and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits of the device when used as intended by the manufacturer;

Definition of Clinical Evaluation

- "clinical data" means information concerning safety or performance that is generated from the use of a device and is sourced from the following:
  - — **clinical investigation(s)** of the device concerned,
  - — **clinical investigation(s) or other studies reported in scientific literature**, of a device for which equivalence to the device in question can be demonstrated,
  - — **reports published in peer reviewed scientific literature** on other clinical experience of either the device in question or a device for which equivalence to the device in question can be demonstrated,
  - — clinically relevant information coming from post-market surveillance, in particular the post-market clinical follow-up

臨床評估


- 臨床試驗
- 臨床試驗或臨床研究科學文獻資料(相等性醫材)
- 同儕評審發表的科學文獻研究報告
臨床資料
臨床評估結果
- 安全性資料
- 功效性資料
- 臨床效益資料
上市後監督資料
上市後臨床追蹤資料

Definition of Clinical Evaluation

- ‘clinical evidence’ means clinical data and clinical evaluation results pertaining to a device of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer

Definition of Clinical Evaluation

- "Clinical Safety" The absence of unacceptable clinical risks, when using the device according to the manufacturer's Instructions for Use;

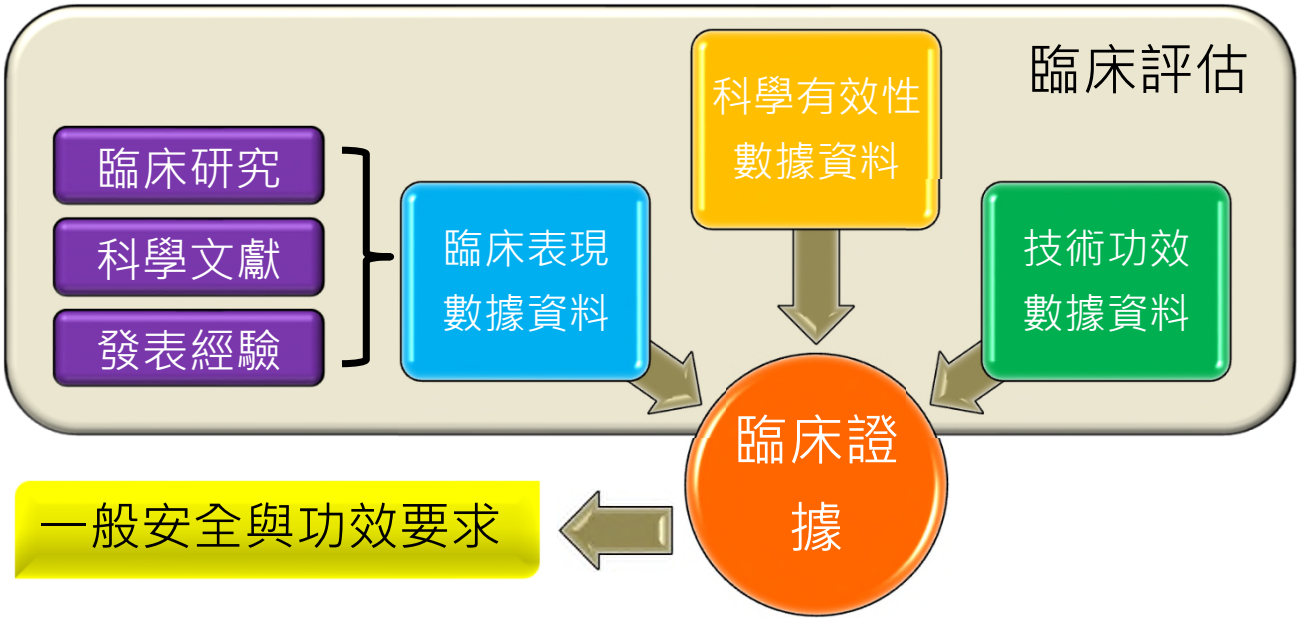
- "Clinical Performance" means the ability of a device, resulting from any direct or indirect medical effects which stem from its technical or functional characteristics, including diagnostic characteristics, to achieve its intended purpose as claimed by the manufacturer, thereby leading to a clinical benefit for patients, when used as intended by the manufacturer;

Definition of Clinical Evaluation

- “clinical benefit” means the positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health;

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 臨床評估 (Article 61)**



臨床評估的執行

臨床評估應根據以下內容，遵循一個明確且方法具體的合理程序 (Article 61)

- 目前可得與此醫療器材的安全、效能、設計特性與預期使用目的相關的科學文獻之關鍵性評估，並須滿足以下條件:
  - 根據附錄XIV的第三節，顯示針對其預期使用目的進行臨床評估的醫療器材，與(引用)相關資料的醫材具有相等性；
  - 收集的文獻資料充分顯示符合通用安全與效能要求(GSPR)
- 針對所有臨床試驗結果進行關鍵性評估，並且考量此臨床試驗是否依據第62條至80條，根據第81條及附錄XV通過之法案；以及
- 考量目前針對此預期目的之可行替代療法選項 – benefit ?

臨床評估的執行

- 對於植入式和第三等級器材，應進行臨床試驗，除非：
  - 此器材係由同一製造商對已上市的器材進行設計修改，
  - 修改後的器材已由該製造商證明等同於已上市的器材；符合附錄XIV第三章要求且經驗證單位審查核可，並且
  - 已上市器材的臨床評估能充分證明經修改的器材符合相關安全與功效要求
- 在此情況下，驗證單位應檢查其PMCF計劃是否適當，並包括上市後研究以證明器材的安全性和功效性；
- 此外，依據Article 61第6節描述之狀況，器材可不須執行之臨床試驗

臨床評估的執行

- 製造商欲證明其器材與非其製造之已上市器材之相等性，亦可依第4節之規定並符合下列條件，免除臨床試驗 ：
  - 兩家製造商已簽訂合約，確保第二個器材的製造商可持續完整取得(已上市器材的)技術文檔；並且
  - 原臨床評估已按照本法規之要求執行
- 第二個器材的製造商提供明確的證據予驗證單位審查；

臨床評估的執行

- 第4節臨床試驗的要求於下列情況，不適用於植入式和第三等級器材：

  （a）已根據指令90/385/EEC或指令93/42/ EEC合法投放市場或投入使用，並且其臨床評估為：

  - 基於充分的臨床資料，並且
  - 此類特定器材已有CS的情況下，其臨床評估符合CS的要求； 或者

  （b）縫線，縫合釘，牙齒填充物，牙齒矯正器，牙冠，螺釘，楔形物，(骨)板，電線，(骨)針，夾子或連接器的臨床評估是基於充分的臨床資料並符合相關產品特定的CS,當特定產品已有CS情況時。

臨床評估的執行

- 對於附件XVI中所列無預期醫療用途的產品，根據本章以及附件XIV和XV證明具有臨床利益的要求應視為證明器材性能的要求。 這些產品的臨床評估應基於有關安全性的相關資料，包括來自上市後監督，PMCF的資料，以及（如適用）特定的臨床試驗。 除非有充分理由依靠類似醫療器材的現有臨床資料，否則應對這些產品進行臨床試驗。

臨床評估

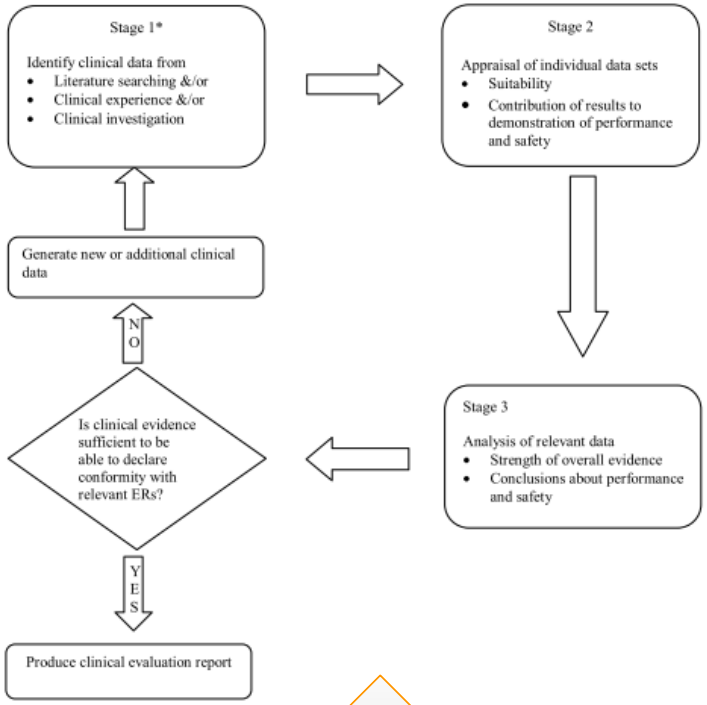
- **醫療器材法規 (MDR, EU 2017/745) 之臨床評估**
  - 醫療器材**臨床評估**是一個數據評估和分析的連續過程，可用於說明製造商的預期用途的產品臨床表現數據、科學有效性數據和技術功效數據。
  - 臨床評估所得到的數據及資訊，可用以提供產品的**臨床證據**。
  - 臨床評估應客觀考慮**有利及不利**的數據。
  - 臨床評估執行的深度和程度應與**醫材的特性**相符一致。例: 風險、分類等級、功效、預期目的。
  - 製造商須制訂臨床評估**計畫**。

臨床評估

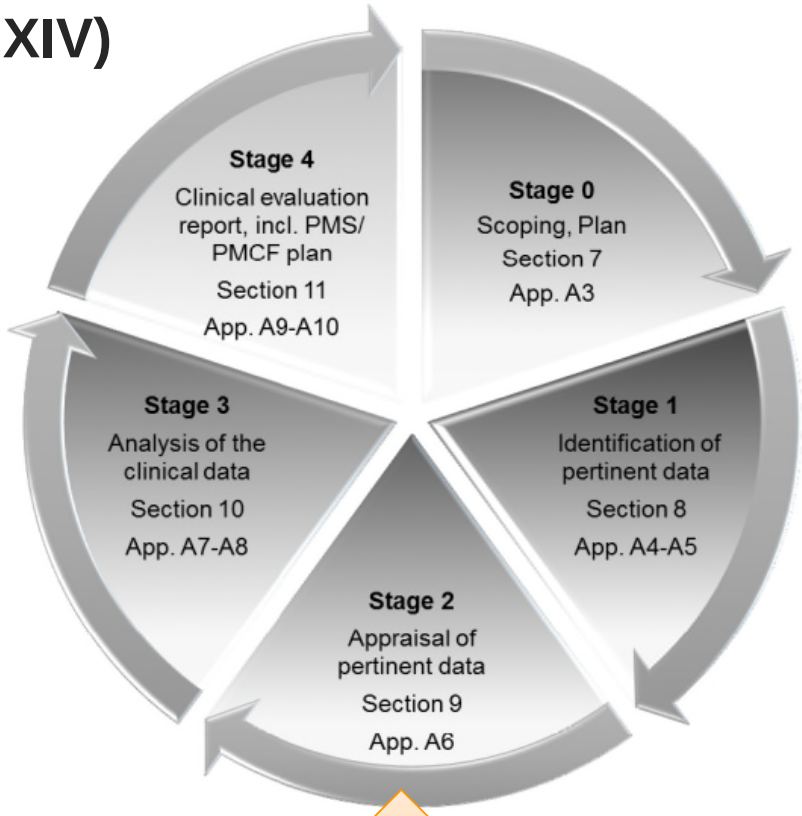
- **醫療器材法規 (MDR, EU 2017/745) – 臨床評估 (Article 61)**
  - 臨床評估及其報告應在醫療器材的整個生命週期內，根據上市後臨床追蹤計劃和上市後監督計劃獲得的數據，予以更新。
  - Class III類別和植入性(Implantable)類別等級醫療器材的臨床評估報告必要時需即時進行更新，但至少應每年更新一次安全與臨床功效性摘要(**SSCP**)。
  - 除客製化器材外，臨床評估其結果和其衍生的臨床證據應記錄在附錄XIV第4節所指的臨床評估報告中，且應為附錄II技術文件之一部分。

臨床評估

- 醫療器材法規 (MDR, EU 2017/745) – 臨床評估 (Article 61 & Annex XIV)



MEDDEV 2.7/1 Rev.3



MEDDEV 2.7/1 Rev.4

臨床評估-MEDDEV 2.7/1 REV.4與MDR

- **參考: MDCG 2020-6，Appendix I**
  - **6.4. Who should perform the clinical evaluation?**
  - **8. Identification of pertinent data (Stage 1)**
  - **9. Appraisal of pertinent data (Stage 2)**
  - **10. Analysis of the clinical data (Stage 3). This chapter includes references to the MDD, MDR requirements should be used instead**
  - **A3. Device description - typical contents**
  - **A4. Sources of literature**
  - **A5. Literature search and literature review protocol, key elements**
  - **A6. Appraisal of clinical data - examples of studies that lack scientific validity for demonstration of adequate clinical performance and/or clinical safety**
  - **A7.2. Conformity assessment with requirement on acceptable benefit/risk profile**
  - **A7.3. Conformity assessment with requirement on performance**
  - **A7.4. Conformity assessment with requirements on acceptability of undesirable side-effects**
  - **A10. Proposed checklist for the release of the clinical evaluation report.**

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 臨床評估 (Annex XIV Part A)**
  - 臨床評估**計畫**至少須包含:

  (a)

  ① 鑑別出安全與功效需求中(GSPR)所必須符合部分。

  ② 醫材預期目的及預期用途。

  ③ 適用族群其明確適應症與禁忌症之清楚規格。

  ④ 關於病患臨床療效與相關/特定臨床參數之清楚描述

  ⑤ 對臨床安全性的定性和定量方面進行檢查的方法規範，明確指出殘留風險和副作用的決定。。

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 臨床評估 (Annex XIV Part A)**
  - ⑥ 根據醫學的最新工藝建立的參數指示的清單及規格用於決定器材預期用途/用途的各種適應症的受益風險比的可接受度 。
  - ⑦ 指示如何處理與特定成分（例如，使用藥物，非活性的動物或人體組織）有關的利益風險問題；和
  - ⑧ 臨床開發計劃，指示從探索性研究（例如，第一人稱研究，可行性研究和試點研究）發展到確認性研究（例如關鍵臨床研究）和本附件B部分中提到的PMCF和以下指示：里程碑和潛在接受標準的描述；。

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 臨床評估 (Annex**

  （b）通過系統的科學文獻綜述，確定與該器材及其預期用途相關的可用臨床數據以及臨床證據中的任何空白；

  （c）通過評估所有相關臨床數據對確定該裝置的安全性和性能的適用性進行評估；

  （d）根據臨床發展計劃，通過適當設計的臨床研究，產出因應重要未決問題所需的任何新的或補充的臨床資料；

  （e）分析所有相關的臨床數據，以便得出有關該設備的安全性和臨床性能（包括其臨床益處）的結論。

  。

臨床評估

- 醫療器材法規 (MDR, EU 2017/745) – 臨床評估報告

Table of Contents	Examples of Contents
1. Summary	Executive summary, the determination of the benefit/risk profile.
2. Scope of the clinical evaluation	Please refer to Section 7 and Appendix A3: Identification of devices, concise physical and chemical description, technologies, etc.
3. Clinical background, current knowledge, state of the art	Please refer to Section 8-10 and Appendices A4-A5: Brief summary and justification of the literature search, applicable standards and guidance, available therapeutic/diagnostic options.
4. Device under evaluation **4.1 Type of evaluation** **4.2 Demonstration of equivalence (only when equivalence is claimed)** **4.3 Clinical data generated and held by the manufacturer** **4.4 Clinical data from literature** **4.5 Summary and appraisal of clinical data** **4.6 Analysis of the clinical data** **4.6.1 Requirement on safety** **4.6.2 Requirement on acceptable benefit/risk profile** **4.6.3 Requirement on performance** **4.6.4 Requirement on acceptability of side-effects**	Type of clinical evaluation (scientific literature, investigations, conformity of essential requirements/general safety and performance requirements) Please refer to Appendix A1, and MDCG 2020-5 for demonstration of equivalence: AND Section 3 of MDR; Please refer to Section 8.1, 8.2 and Appendices A4-A5 for clinical data; Please refer to Section 9 and Appendix A6 for appraisal of clinical data; Please refer to Section 10 and Appendix A7 for essential requirements/general safety and performance requirements.
5. Conclusions	Please refer to Section 11 of the statement of compliance.
6. Date of the next clinical evaluation	Please refer to Section 6.2.3 on suggested date, justification of the date.
7. Dates and signatures	Please refer to Section 11.
8. Qualification of the responsible evaluators	Please refer to Section 6.4 for details.
9. References	Please refer to Section 11.

Appendix 9, MEDDEV 2.7/1 rev.4

臨床評估

- 醫療器材法規 (MDR, EU 2017/745) – 臨床評估評鑑報告

A12.2 of MEDDEV 2.7/1 rev.4 (2016)	Template of CEAR (MDCG 2020-13)
A12.2.1. Decision-making by the notified body **A12.2.2. The report of the notified body** **- device description and product specification** **- intended purpose of the device** **- classification proposed for the device** **- pre-clinical evaluation data presented by the manufacturer** **- risk analysis and risk management and alignment with the clinical evaluation report** **- clinical evaluation process** **- clinical evaluation report authors** **- equivalence assessment – if data from equivalent is used** **- clinical investigation plans and reports** **- justification if no clinical investigation has been performed** **- instructions for use, labelling and, when necessary, the training plan for users** **- justification if no PMCF is planned** **- PMS** **- PMCF** **- planned frequency/ criteria for updates to the clinical evaluation** **- summary of review** **- conclusion on clinical benefit/risk profile** **- conformance of the device to the relevant Essential Requirements**	Section A: Administrative particulars (notified body, manufacturer, product and clinical evaluation report reference) Section B: Reviewers involved in the notified body assessment of the clinical evaluation Section C: Device description, classification, clinical evaluation plan, information materials supplied by the manufacturer, common specifications and harmonised standards applied, equivalence and state of the art Section D: Clinical literature review Section E: Clinical investigations and related documentation Section F: PMS, PMCF and the plan for updates Section G: IFU, SSCP, labelling and other information supplied with the device Overall Conclusions: Section H: Summary of all available data and conclusions Specific Considerations: Section I: Clinical evaluation consultation procedure for certain class III and class IIb devices (Article 54) Section J: Where demonstration of conformity based on clinical data is not deemed appropriate (Article 61(10)) Section K: The voluntary clinical consultation on the clinical development strategy (Article 61(2))

MDCG 2020-13 CEAR

臨床評估

- **MDCG 2020-13**

A clinical evaluation assessment report (CEAR) is a report used by the notified body to clearly document the conclusions of its assessment of the clinical evidence presented by the manufacturer in the clinical evaluation report (CER) and the related clinical evaluation that was conducted – a core requirement of the Medical Device Regulation (EU) 2017/745 (MDR).

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 臨床試驗 (Article 62)**
  - 臨床試驗的目的在於建立或確認醫材的功效，而其功效的確認無法透過分析研究、文獻或是常規診斷測試來獲得。
  - 執行臨床試驗的數據為用以佐證臨床安全與功效的證據。
  - 臨床試驗各步驟應根據公認的倫理原則進行。
  - 臨床試驗的設計應使數據的相關性最大化，潛在偏差最小化。
  - 臨床試驗應制定臨床試驗計畫(CIP) (Annex XV, EN ISO14155)

(MDCG 2020-10-2 Clinical Investigation Summary Safety Report)

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 上市後臨床追蹤 (Annex XIV)結果與報告**
  - 製造商應分析PMCF的結果，並在PMCF評估報告中紀錄結果。
  - PMCF評估報告應更新臨床評估報告並作為技術文件的一部分。
  - 臨床評估以及風險管理應考慮PMCF評估報告的結論。
  - 經由PMCF的結論，確認需要矯正預防措施，則製造商應確實執行。
  - 若認為PMCF不適用於某特定醫材，則應在臨床評估報告中解釋正當理由。

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 相等性之展現**
  - Technical characteristics:
  - Biological characteristics:
  - Clinical characteristics

MDR Annex XIV Section 3	MEDDEV 2.7/1 rev.4
A clinical evaluation may be based on clinical data relating to a device for which equivalence to the device in question can be demonstrated. The following technical, biological and clinical characteristics shall be taken into consideration for the demonstration of equivalence.	For assuming equivalence, • equivalence can only be based on a single device - all three characteristics (clinical, technical, biological) need to be fulfilled; - similar means that no clinically significant difference in the performance and safety of the device would be triggered by the differences between the device under evaluation and the device presumed to be equivalent.

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 相等性**
  - Technical characteristics:

MDR Annex XIV Section 3	MEDDEV 2.7/1 rev.4
— Technical: the device is of similar design; is **used under similar conditions of use**; has similar specifications and properties including physicochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and **software algorithms**; uses similar deployment methods, where relevant; has similar principles of operation and critical performance requirements;	• Technical: - be of similar design, and - **used under the same conditions of use**, and - have similar specifications and properties (e.g. physicochemical properties such as type and intensity of energy, tensile strength, viscosity, surface characteristics, wavelength, surface texture, porosity, particle size, nanotechnology, specific mass, atomic inclusions such as nitrocarburising, oxidability), and - use similar deployment methods (if relevant), and - have similar principles of operation and critical performance requirements.

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 相等性**
  - Biological characteristics:

MDR Annex XIV Section 3	MEDDEV 2.7/1 rev.4
— Biological: the device **uses the same materials** or substances in contact with the same human tissues or body **fluids for a similar kind and duration of contact and similar release characteristics of substances, including degradation products and leachables;**	• Biological: **Use the same materials** or substances in contact with the same human tissues or body fluids. **Exceptions** can be foreseen for devices in contact with intact skin and minor components of devices; in these cases risk analysis results may allow the use of similar materials taking into account the role and nature of the similar material. Different aspects of equivalence and compliance to different Essential Requirements can be affected by materials.

臨床評估

- **醫療器材法規 (MDR, EU 2017/745) – 相等性**
  - Clinical characteristics

MDR Annex XIV Section 3	MEDDEV 2.7/1 rev.4
— Clinical: the device is used for the **same clinical condition or purpose**, including similar severity and stage of disease, at the same site in the body, in a similar population, including as regards age, anatomy and physiology; **has the same kind of user**; has similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.	• Clinical: - used for the same clinical condition (including when applicable similar severity and stage of disease, **same medical indication**), and - used for the same intended purpose, and - used at the same site in the body, and - used in a similar population (this may relate to age, **gender**, anatomy, physiology, possibly other aspects), and - not foreseen to deliver significantly different performances (in the relevant critical performances such as the expected clinical effect, the specific intended purpose, the **duration of use**, etc.).

醫療器材相等性比較表

- 參考: **Annex I of MDCG 2020-5 Equivalence table**

Equivalence table **for the comparison of a device with a presumed equivalent marketed device for the purpose of demonstrating equivalence**			
1. Technical characteristics (add a separate row for each of the assessed characteristics)	**Device 1 (under clinical evaluation)** Description of characteristics and reference to specifying documents	**Device 2 (marketed device)** Description of characteristics and reference to specifying documents	**Identified differences or conclusion that there are no differences in the characteristic**
Device is of similar design			1.1
Used under similar conditions of use			1.2
Similar specifications and properties including physiochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and			1.3

Annex I – Equivalence table, MDCG 2020-5

宣稱臨床相等性常見問題

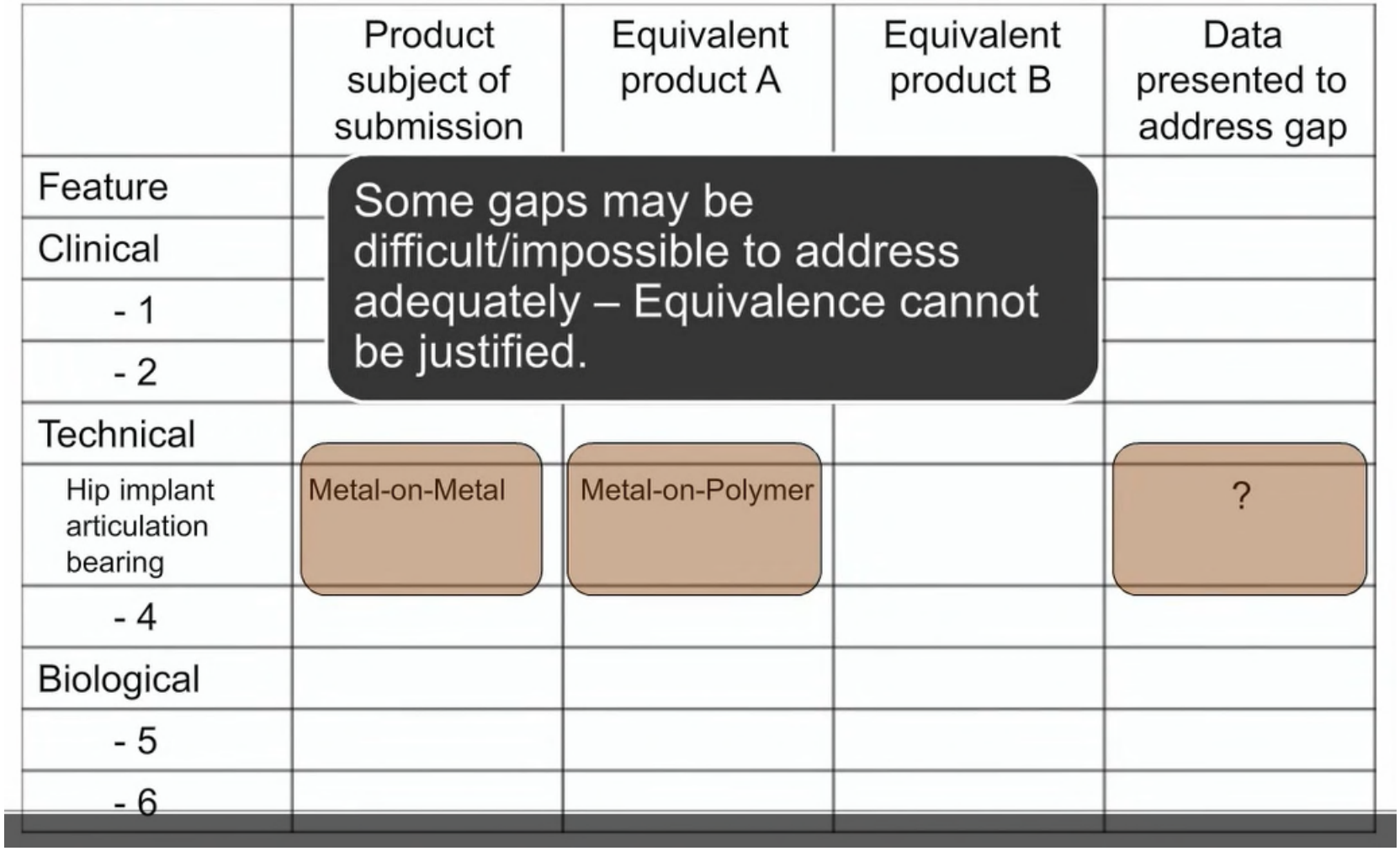
SGS

COMMON PROBLEM AREAS - EQUIVALENCE JUSTIFICATION

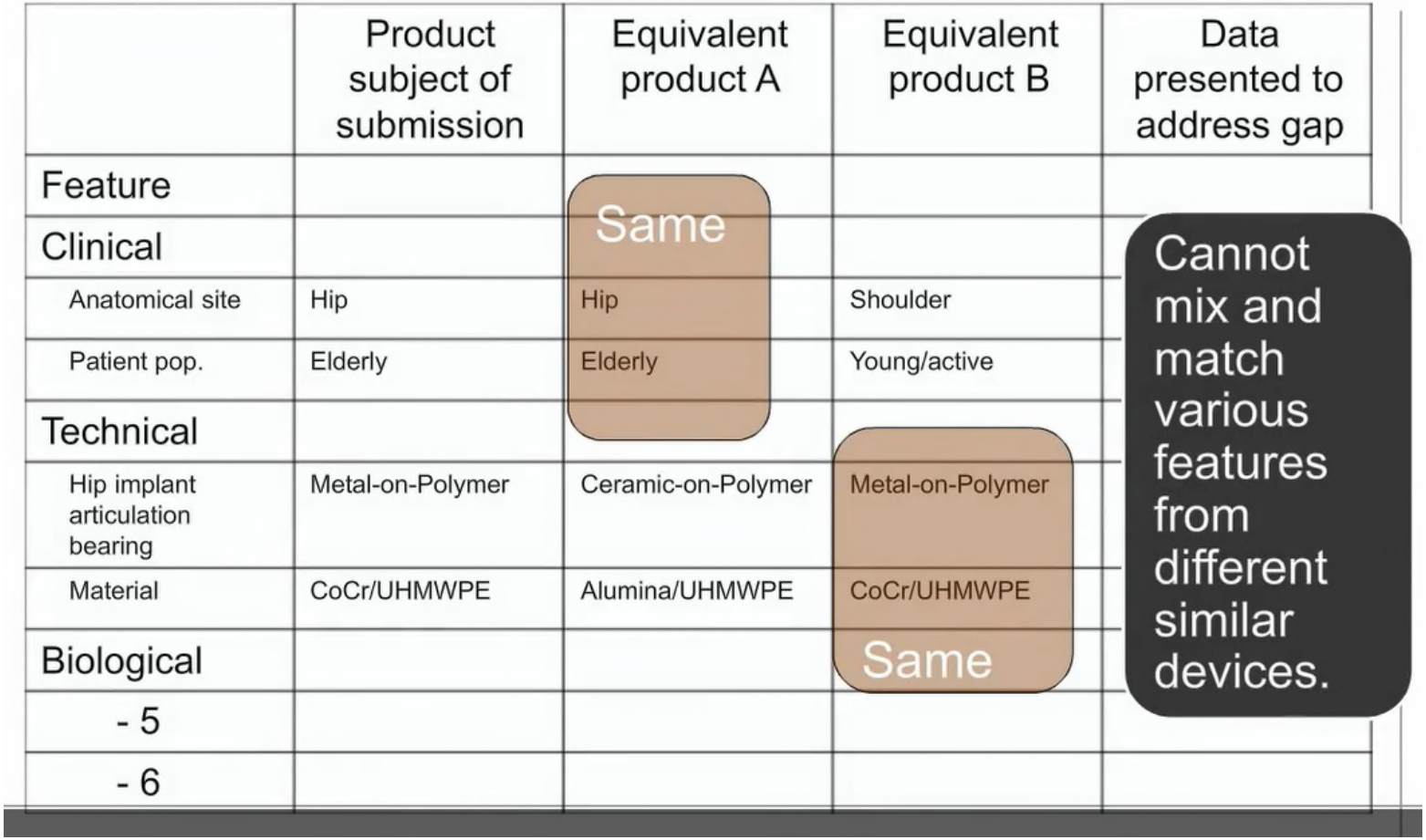
	Product subject of submission	Equivalent product A	Equivalent product B	Data presented to address gap
Feature				
Clinical				
- 1				
- 2				
Technical				
Material	Titanium	Titanium alloy		?
- 4				
Biological				
- 5				
- 6				

All gaps must be adequately addressed

宣稱臨床相等性常見問題



宣稱臨床相等性常見問題



臨床評估-LEGACY DEVICES

- 名詞定義與解釋 (MDCG 2020-6)
  - Legacy devices定義: 已根據指令90/385/EEC或指令93/42/EEC合法上市器材;
  - Sufficient clinical evidence解釋: 符合要求的評鑑之目前結果，已對器材是安全且能達成其預期使用利益完成結論。
- 已上市器材免除臨床試驗的條件
  - 基於充分的臨床資料，並且
  - 此類特定器材已有CS的情況下，其臨床評估符合CS的要求；
- 一般方面(aspect)的要求
  - ✓一MDR要求建立上市後資料(包括上市後臨床追蹤)、臨床評估計畫與報告;
  - ✓充分的臨床資料顯示符合MDR GSPR要求

Article 61(6) of MDR, MDCG 2020-6

臨床評估-LEGACY DEVICES

- 特別面向(aspect)要求 (MDCG 2020-6 & MDR附錄XIV Part A)
  - 建立或更新臨床評估計畫；
  - 鑑別可取得的臨床資料
    - 上市前臨床資料資源
    - 上市後臨床資料資源
  - 臨床資料評價；
  - 新臨床資料的產出；
  - 臨床資料的分析

Article 61(6) of MDR, MDCG 2020-6

臨床評估-LEGACY DEVICES

- MDCG 2020-6 Appendix II: 適用於先前已上市器材的臨床評估計畫至少應包含
  - 鑑別GSPR中需要相關臨床資料支持的章節；
  - 評估中器材之預期使用目的相關細節規格特性；(註labelling)
  - 目標使用族群、包括其詳盡的適應症與禁忌症的詳細清楚規格特性
  - 對病患預期使用臨床效益、以及特別的臨床結果參數之詳細描述
  - 鑑別、分析及評估替代療法的策略；
  - 明確參考殘餘風險和副作用之決定、以定性及定量檢驗臨床安全性 的方法之詳細規格特性

Appendix II of MDCG 2020-6

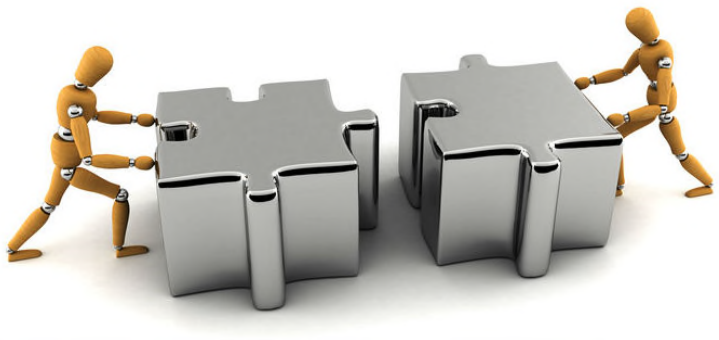
臨床評估-LEGACY DEVICES

- MDCG 2020-6 Appendix II: 適用於先前已上市器材的臨床評估計畫至少應包含
  - 一個 基於醫藥的最新工藝、考量眾多適應症以及該器材預期使用目的之利益-風險可接受度 的指示性清單及用以決定的參數之規格特性 ；
  - 如何解決/界定關於特定成分例如藥品、非活性動物或人類組織的使用之利益-風險議題的指示；
  - 按照已變更定義的臨床資料，用以鑑別、分析以及評價所有可取得的臨床資料之策略與方法；
  - 相等性的證據(若臨床評估內含有相等器材的臨床資料)；
  - 臨床證據的所需等級的定義(應與器材及其預期使用目的特性等比例)；
  - 系統化收集、摘要與取用上市後監督資料之策略與方法學，以呈現持續的安全性及功效性，以及該已上市器材延伸之關於安全及功效的抱怨已被發現。

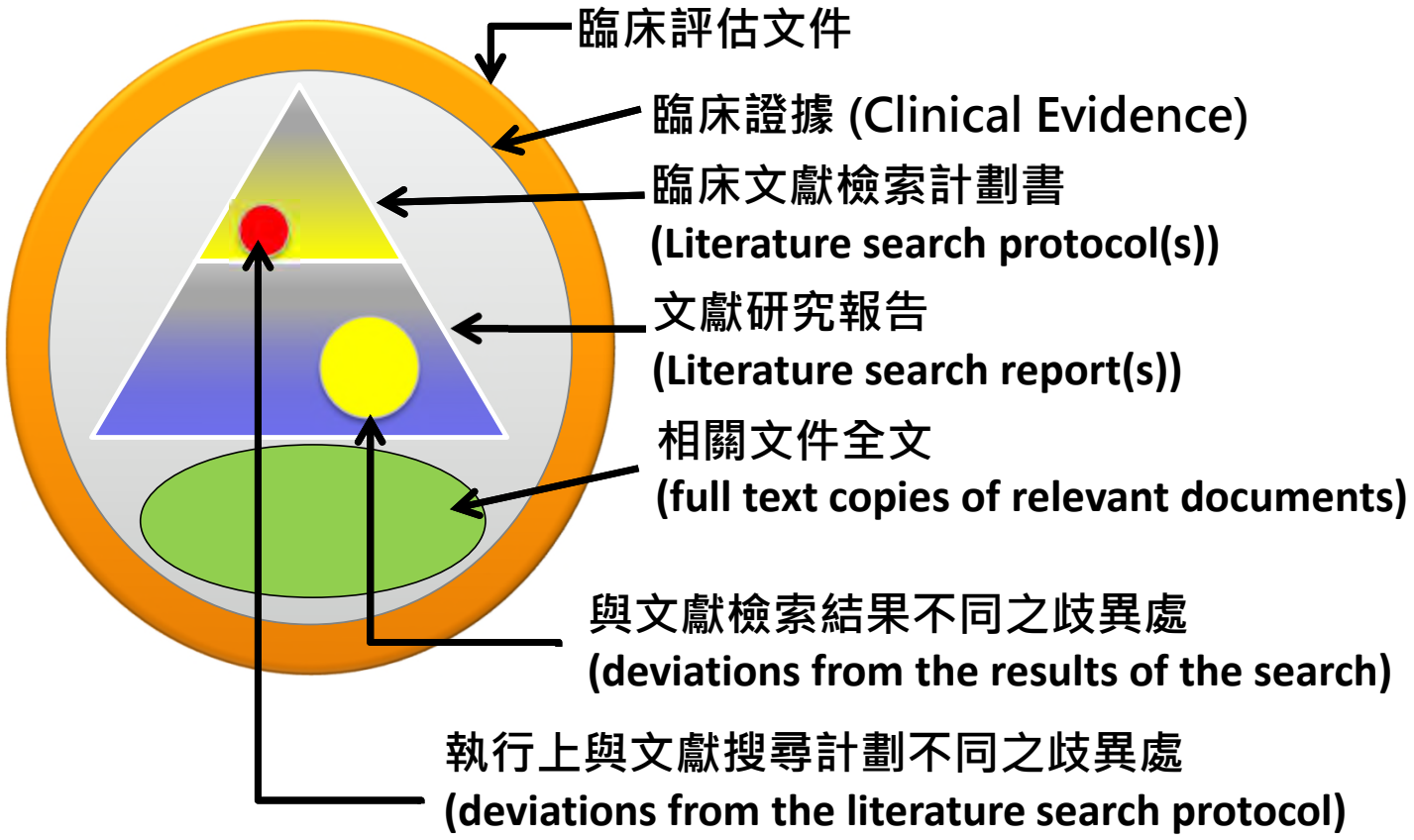
Appendix II of MDCG 2020-6

臨床評估之文獻檢索指引實作

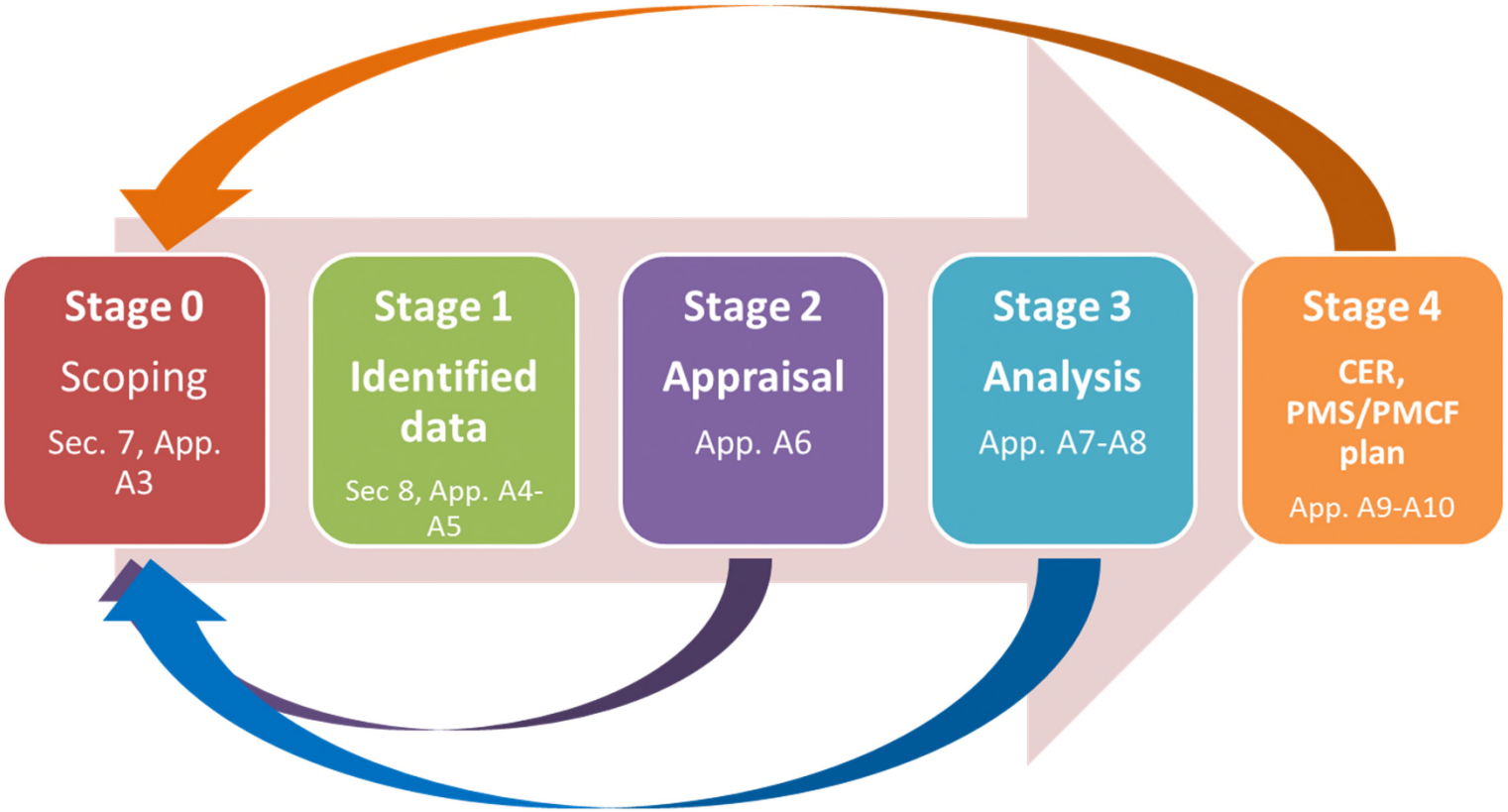
(MEDDEV 2.7/1 REV.4)



臨床評估相關文件示意圖



Stages of Clinical Evaluation



Ref: Figure of MEDDEV 2.7/1 revision 4

THE CLINICAL EVALUATION REPORT

MEDDEV2.7/1 REV.4 SECTION 11

- Stage 0, scope of the clinical evaluation:
  - explains the scope and context of the evaluation, including which products/ models/sizes/ settings are covered by the clinical evaluation report, the technology on which the medical device is based, the conditions of use and the intended purpose of the device;
  - documents any claims made about the device's clinical performance or clinical safety

Stage 0 – Scoping and Planning

example of clinical evaluation plan

Aspects ***(note: not an exhaustive list)***	**Before CE**	**CE marked**
Device description	**X**	**X**
Design features, indications, target population, specific claims	**X**	**X**
Information of Equivalence (if claimed)	**X**	
Risk management documents of the device e.g. the hazard identification list, clinical risks identified from the risk analysis.	**X**	**X**
The current knowledge/state of the art such as standards, guidance, benchmark devices and medical alternatives available to the target population.	**X**	**X**
Data sources -generated and held by the manufacturer or available from scientific literature.	**X**	**X**

(next page)

Stage 0 – Scoping and Planning

example of clinical evaluation plan

Aspects ***(note: not an exhaustive list)***	**Before CE**	**CE marked**
Relevant changes, including -design; -material and manufacturing procedures; -information supplied; And, whether the claimed equivalence still appropriate.	**--**	**X**
Newly emerged special clinical concerns	--	**X**
PMS aspects regularly updating in the clinical evaluation report: -new clinical data of the device under evaluation; -new clinical data of the equivalent device (if equivalence is claimed); -new knowledge about known and potential hazards, risks, performance, benefits and claims	--	**X**
Needs for planning PMS activities	--	**X**

THE CLINICAL EVALUATION REPORT

MEDDEV2.7/1 REV.4 SECTION 11

- Stage 1, identification of pertinent data:
  - explains the literature search strategy;
  - presents the nature and extent of the clinical data and relevant pre-clinical data that have been identified

Stage 1 – Identification of Pertinent Data 8.2– Data retrieved from literature

- **Data retrieved from literature**

  Literature searching identifies potential sources of clinical data for establishing:

  - Clinical data relevant to the device under evaluation and relevant equivalent device (if equivalence is claimed)
  - Current knowledge/ the state of the art
  - Several searches with different search criteria or focus are usually necessary to obtain the necessary data. (**Appendix A4: Sources of literature**);
  - A literature search and other retrieval of data are carried out based on a **search protocol** (**Appendix A5: Literature search and literature review protocol, key elements**);

Stage 1 – Identification of Pertinent Data 8.2– Data retrieved from literature (cont'd)

Aspects should be considered for literature searching:

- IMPORTANT: literature search is documented to such degree that the methods can be appraised critically, the results can be verified, and the search reproduced if necessary.

SOURCES OF LITERATURE

- A comprehensive search strategy is required to involve multiple databases as different sources of clinical literature.
- The search strategy should be documented and justified (within the “search protocol”➔ A5.3 Methods).
- Important sources include the following:
  - Scientific literature databases
  - Internet searches
  - ~~*Non-published data*~~

SCIENTIFIC LITERATURE DATABASES

- MEDLINE or Pubmed
  - a good starting point for a search;
  - possibly incomplete coverage of European Journals.
- European Journals/database
  - EMBASE/Excerpta Medica;
  - Cochrane CENTRAL trials register.

SCIENTIFIC LITERATURE DATABASES

- **Internet searches**
  - Harmonised/other standards on clinical performance and clinical safety;
  - Field safety corrective actions for the equivalent and/or other devices (e.g., FDA MAUDE, EU IRIS);
  - Implant registry reports;
  - Documents available in systematic review databases (e.g. the Cochrane Database);
  - Expert documents produced by professional medical associations;
  - Meta-analyses and reviews of health technology assessment (HTA) institutes and networks;
  - WHO International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov

SCIENTIFIC LITERATURE DATABASES

- ~~**Non-published data**~~
  - ~~The label and IFU of the equivalent device (if equivalence is claimed by the manufacturer) and/or of benchmark devices;~~
  - ~~Data provided to manufacturers from implant registries;~~
  - ~~Data presented at congresses (conferences).~~

OUTPUT OF LITERATURE SEARCH AND REVIEW

- Literature on the device in question *and* the equivalent device.
- A review of the current knowledge/the state of the art of the clinical data of the device under evaluation *and* the equivalent device.

  - ✓ The literature collected may relate directly to the device in question* and/or to equivalent device, benchmark devices, other devices and medical alternatives available to the intended patient population.
  - ✓ Following proper appraisal and analysis will be needed.
  - ✓ The selection of literature should be objective and justified, i.e. include all relevant data, both favourable and unfavourable.

Appendix 5 of MEDDEV 2.7/1 rev.4

LITERATURE SEARCH PROTOCOL

- **Methods:** The methods section of the protocol documents
  - the plans for literature search,
  - study selection,
  - data collection, and
  - analysis methods.

  It defines the literature search strategy and the inclusion/exclusion criteria for the documents found.

  Objective, non-biased, systematic search and review methods should be used.

  Examples are:

  ✓ PICO

  ✓ Cochrane Handbook

  ✓ PRISMA

  ✓ MOOSE Proposal

Appendix 5 of MEDDEV 2.7/1 rev.4

LITERATURE SEARCH PROTOCOL

- **Objective**
  - Research question(s) come from device description, intended performance, any claims on clinical performance and clinical safety, and risk management process, should be consistent with the scope of the clinical evaluation;
  - The process should be carefully constructed, e.g. **PICO**:
    - **P**opulation(s)/disease(s) or condition(s)
    - **I**ntervention(s)
    - **C**omparator group(s)/control(s)
    - **O**utcome(s)/endpoint(s)

Appendix 5 of MEDDEV 2.7/1 rev.4

PICO與文獻檢索

- **P-I-C-O:** to define proper clinical research questions
  - P: Problem, Patient, Population, e.g., patient characteristics
  - I: Intervention, Indicator, e.g., type of intervention
  - C: Comparison, Control, e.g., compare to approved device
  - O: Outcome, e.g., pain, fatigue, infections, death, cure

PICO元素	導引出檢索關鍵字
P ➔	
I ➔	
C ➔	
O ➔	

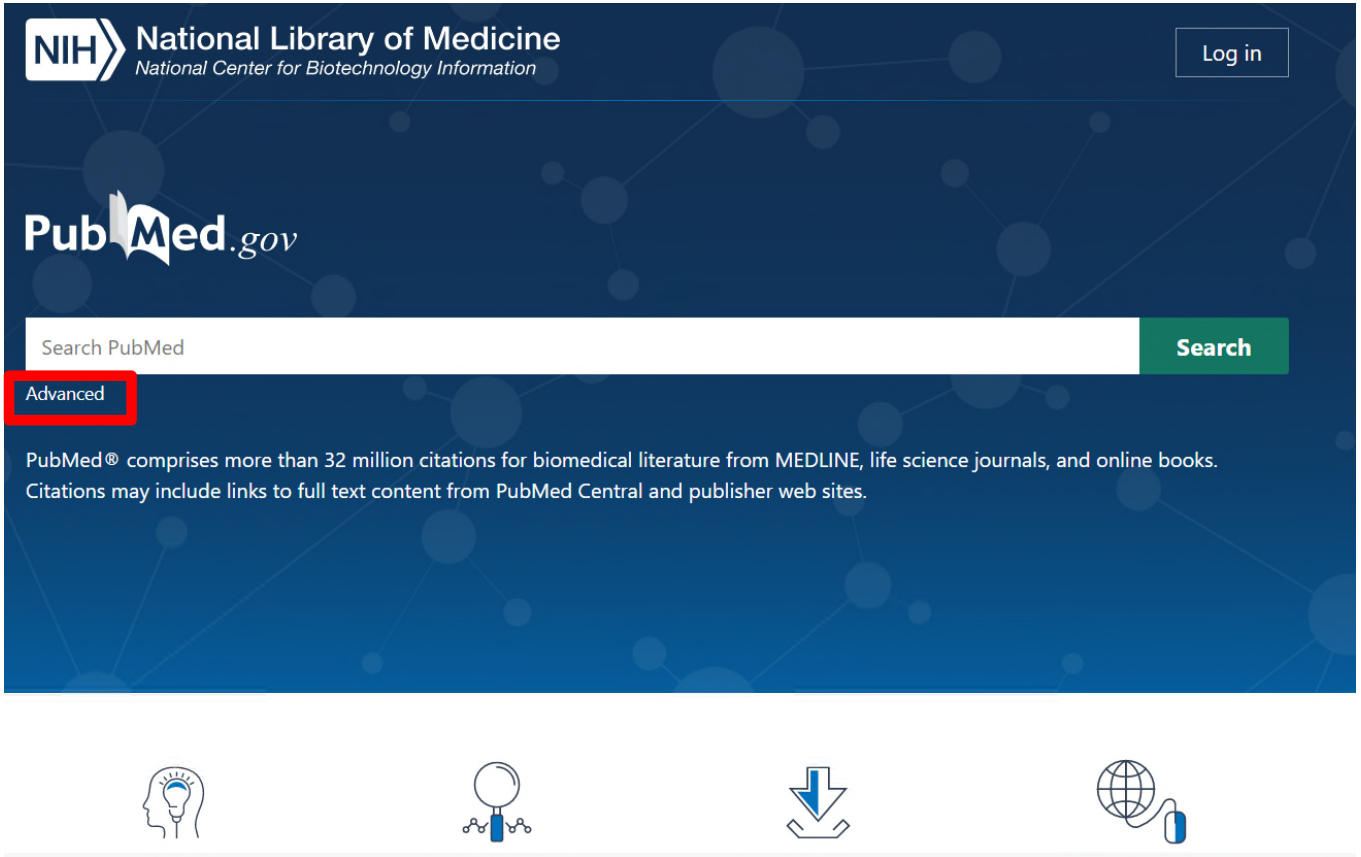
PICO與文獻檢索

- **範例: P-I-C-O 應用於骨科人工肩關節(Shoulder Prosthesis)之臨床評估文獻檢索**
  - P – 骨關節炎、或損傷、或癌症之病患須進行人工關節置換
  - I – 關節置換術、關節重建、反置式肩關節系統
  - C – 目前治療方法、技術之比較
  - O – 療效指標、副作用、併發症、臨床結果

PICO元素	導引出檢索關鍵字
P ➔	Osteoarthritis, traumatic, fracture, bone cancer
I ➔	Replacement, reconstruction, reverse total shoulder arthroplasty
C ➔	Conventional shoulder arthroplasty, shoulder humeral hemiarthroplasty, Arthroscopic
O ➔	Quality of life, pain, infection, recovery rate, mortality

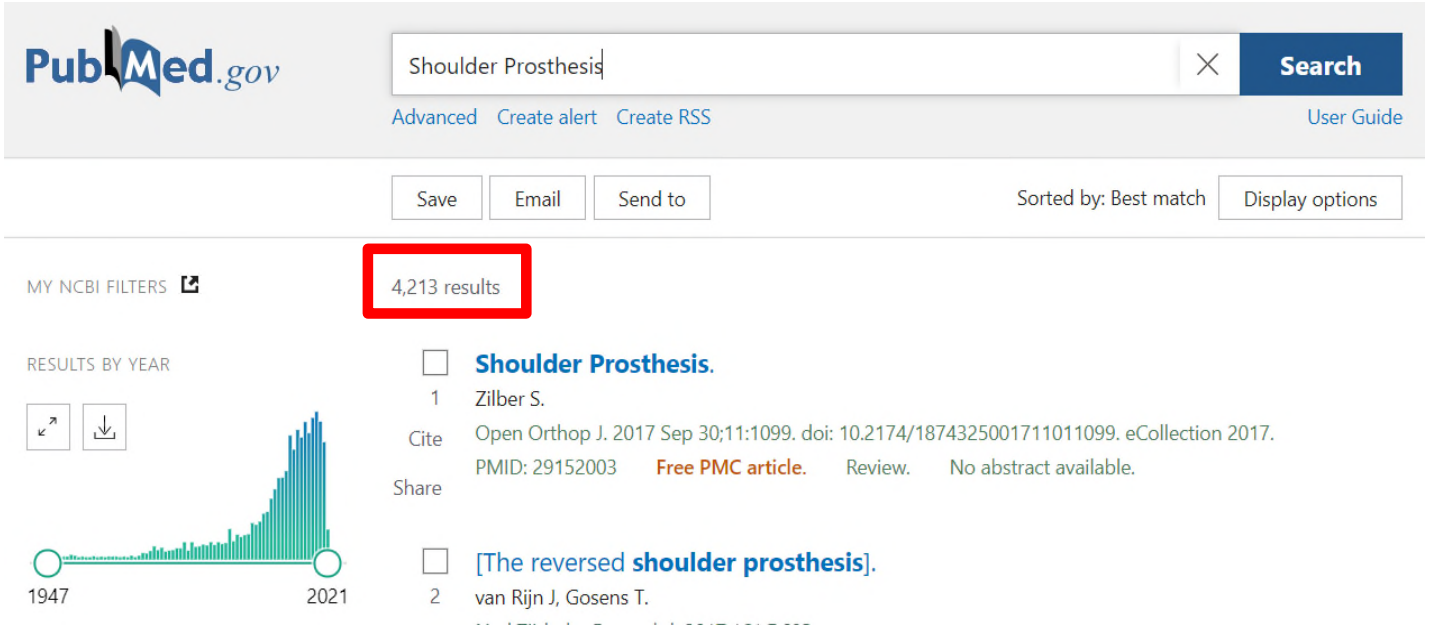
PICO與文獻檢索

- 運用PubMed進行PICO關鍵字文獻搜尋
  - 網址: https://pubmed.ncbi.nlm.nih.gov/ (google: PubMed)



PICO與文獻檢索

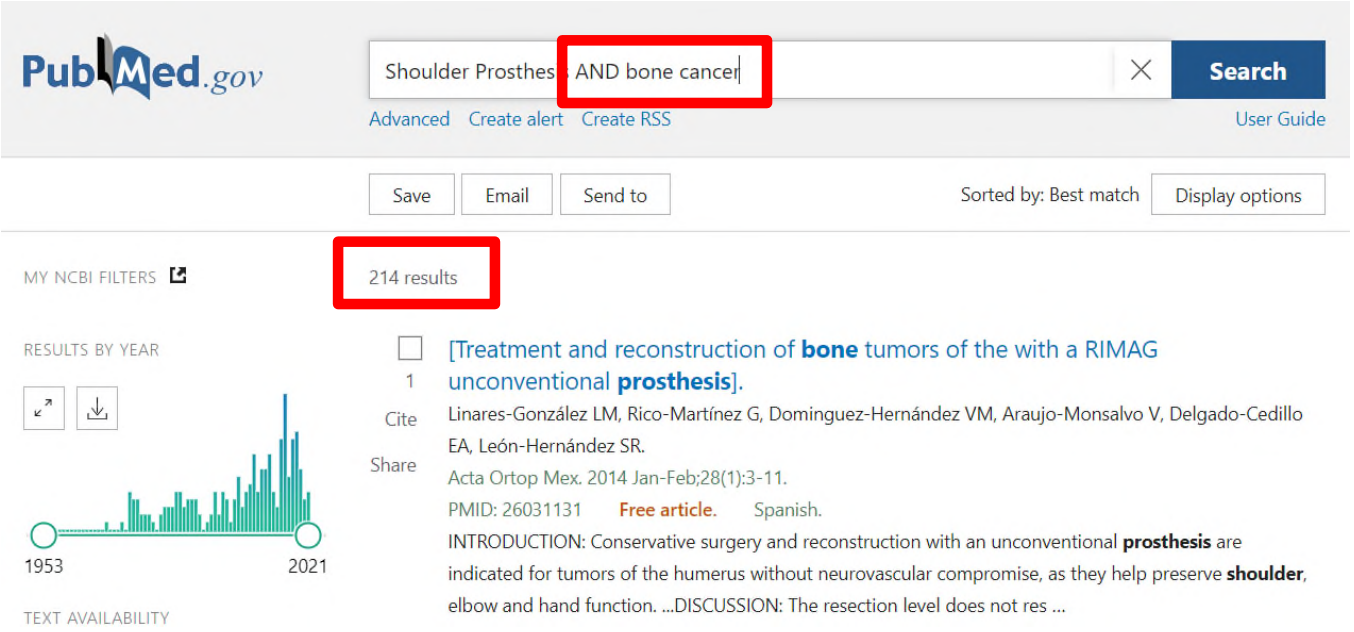
- 運用PubMed進行PICO關鍵字文獻搜尋
  - 網址: https://pubmed.ncbi.nlm.nih.gov/ (google: PubMed)
  - 關鍵字1. Shoulder Prosthesis



PICO與文獻檢索

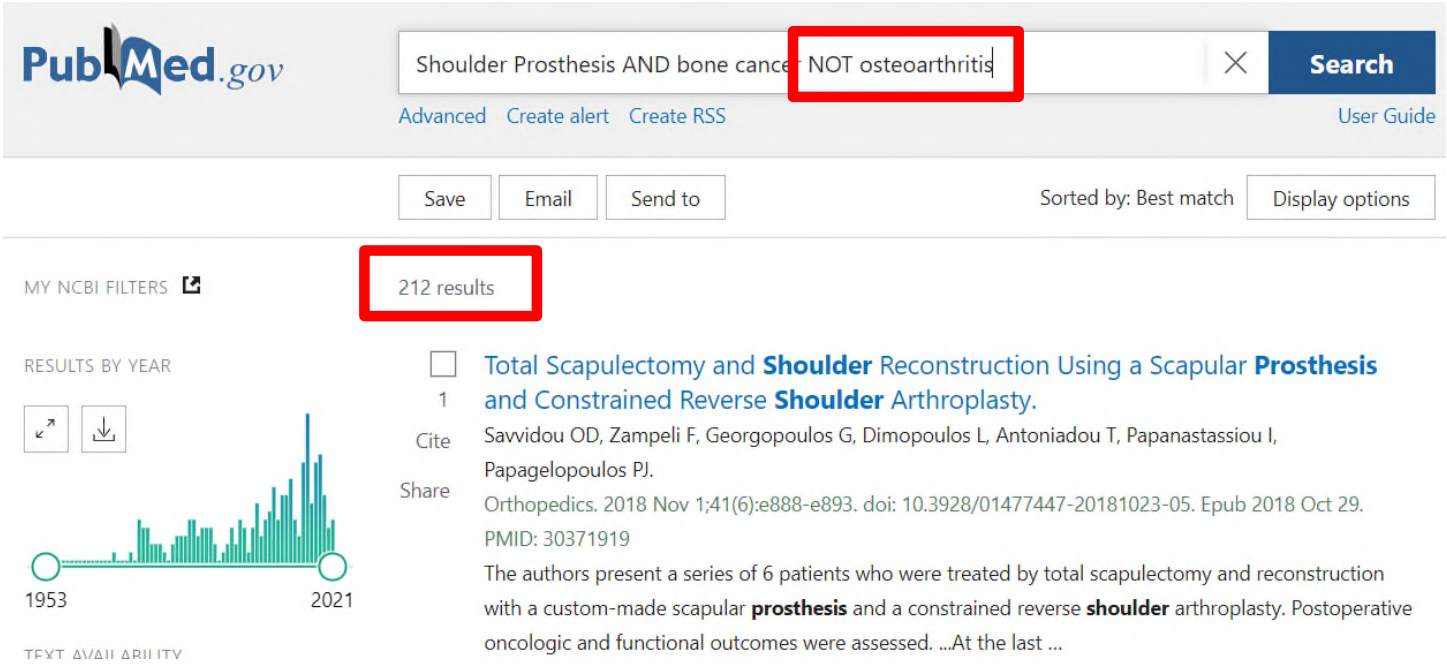
- **運用PubMed進行PICO關鍵字文獻搜尋**
  - 關鍵字2. Shoulder Prosthesis AND bone cancer

Boolean search/布林搜尋
(**AND, OR, NOT**)



PICO與文獻檢索

- 運用PubMed進行PICO關鍵字文獻搜尋
  - 關鍵字3. Shoulder Prosthesis AND bone cancer NOT osteoarthritis



PICO與文獻檢索

- **運用PubMed進行PICO關鍵字文獻搜尋-searching strategy**
  - 在PubMed網址首頁點選ADVANCED

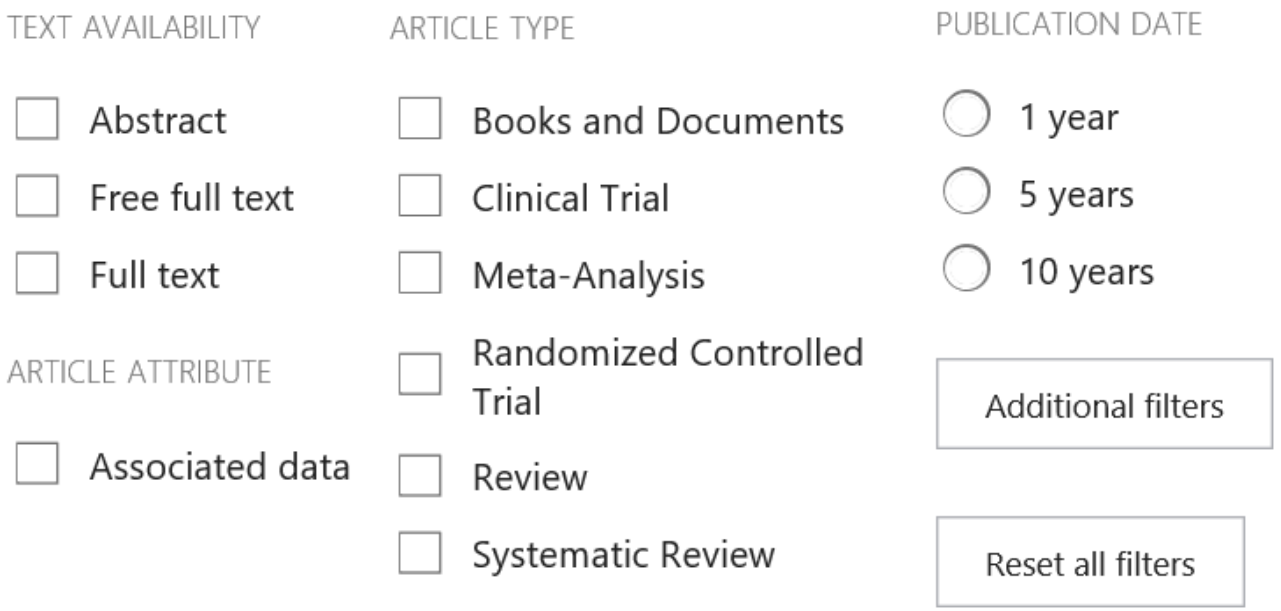
History and Search Details

Download Delete

Search	Actions	Details	Query	Results	Time
#3	•••	›	Search: **Shoulder Prosthesis AND bone cancer NOT osteoarthritis**	212	08:28:35
#2	•••	›	Search: **Shoulder Prosthesis AND bone cancer**	214	08:25:43
#1	•••	›	Search: **Shoulder Prosthesis**	4,213	08:22:12

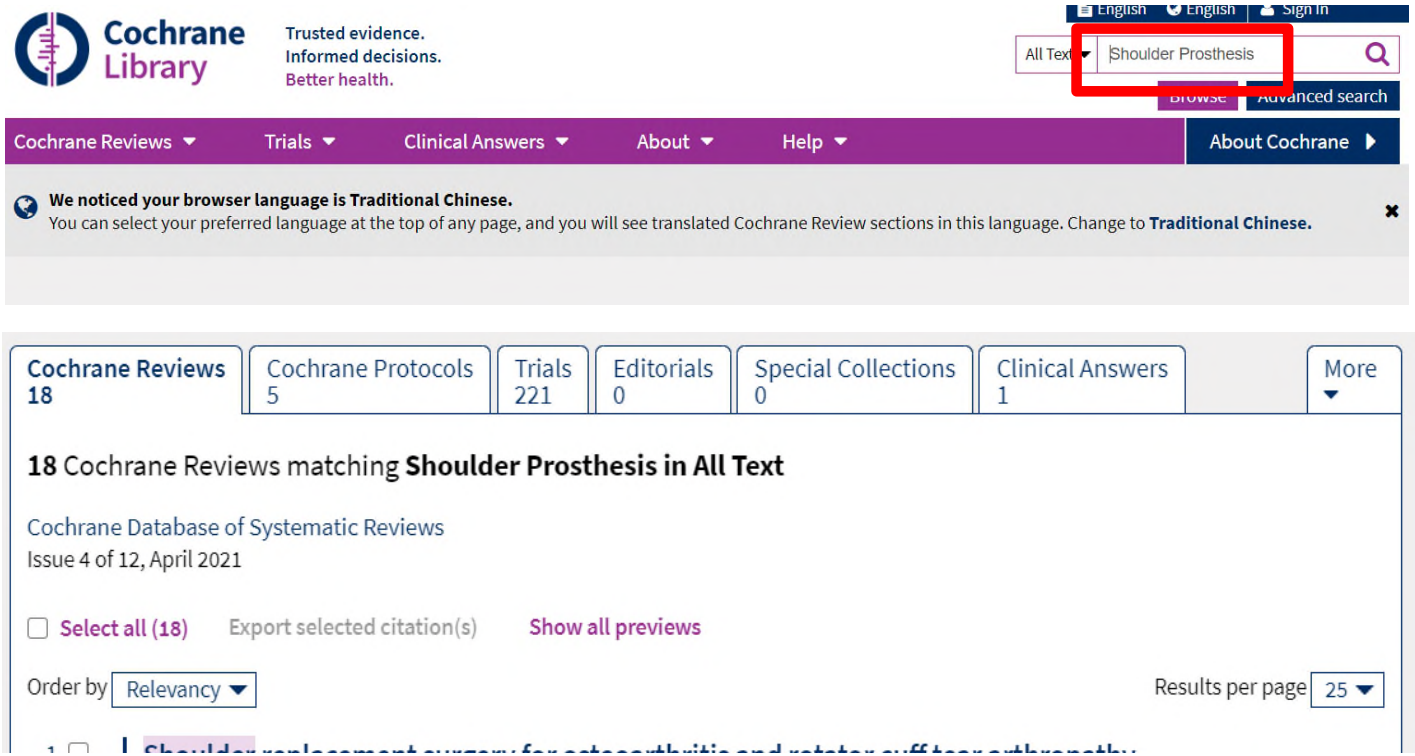
運用PUBMED預設功能篩選檢索文獻類型

- 在PUBMED頁面左邊，可以用來執行篩選功能



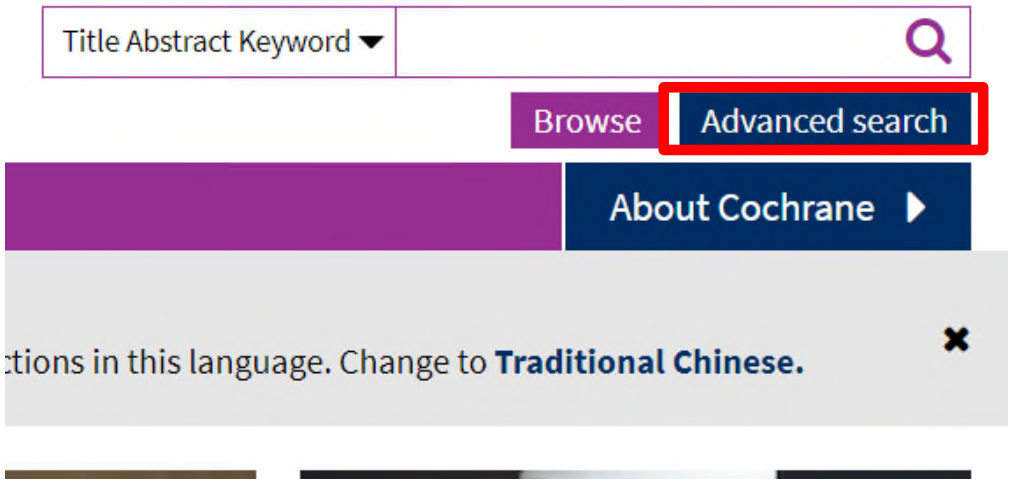
PICO與文獻檢索

- 運用Cochrane進行PICO關鍵字文獻搜尋
  - 網址: https://www.cochranelibrary.com/central (google: Cochrane)
  - 關鍵字1. Shoulder Prosthesis



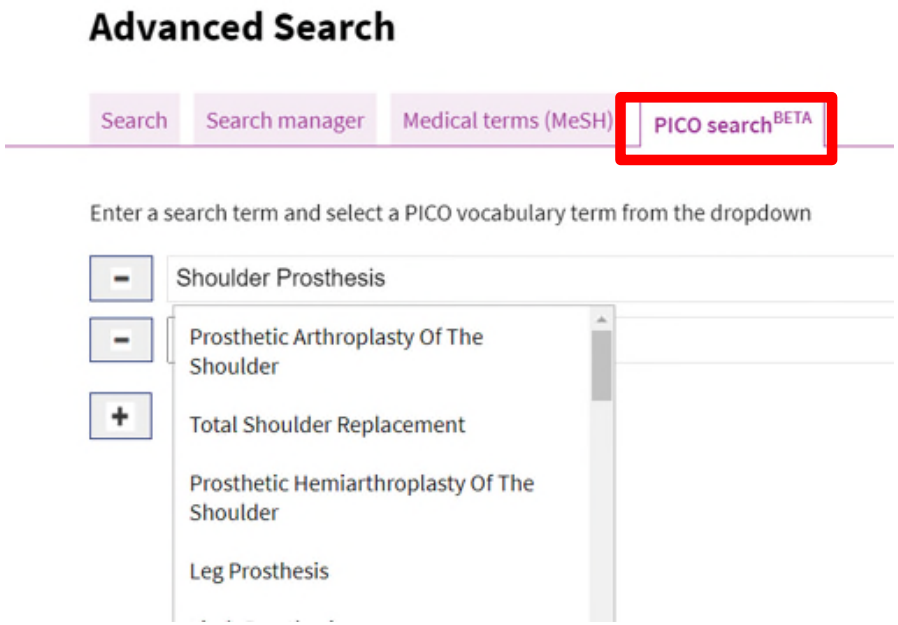
PICO與文獻檢索

- **運用Cochrane進行PICO關鍵字文獻搜尋**
  - 網址: https://www.cochranelibrary.com/central (google: Cochrane)
  - 選用Advanced search功能



PICO與文獻檢索

- 運用Cochrane進行PICO關鍵字文獻搜尋
  - 網址: https://www.cochranelibrary.com/central (google: Cochrane)
  - 在Advanced search模組下直接進行PICO搜尋
  - 輸入關鍵字: Shoulder Prosthesis，系統會自動導引出相關的PICO關鍵字



INTERNET SEARCHES/NON-PUBLISHED DATA

- 以MAUDE (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.CFM)進行檢索
- 搜尋到的結果，可以用來:
  - 尋找產品/類似品的安全與危害相關關鍵字
  - 確定目前相似產品的state of the art

Product Classification

FDA Home ▸ Medical Devices ▸ Databases

1 to 10 of 13 Results
for *Shoulder Prosthesis*

1 2 >

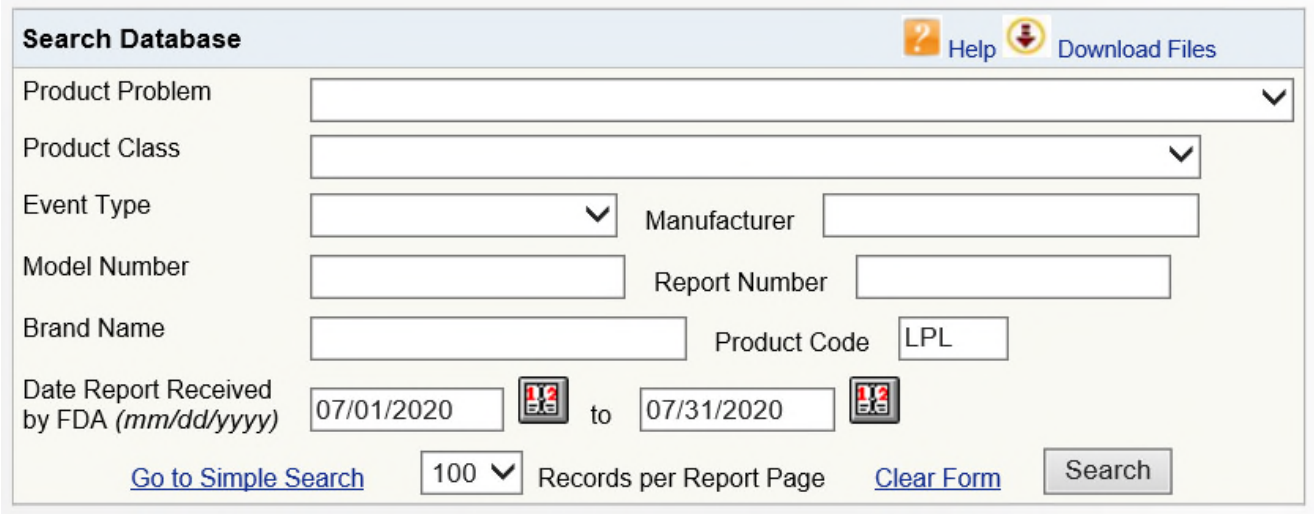
Results per page 10

New Search | Export To Excel | Help

Product Code	Device		Regulation Number	Device Class
HSD	Prosthesis, Shoulder, Hemi-, Humeral, Me ...	Shoulder Joint Humeral (Hemi-Shoulder) M...	888.3690	2
KWR	Prosthesis, Shoulder, Constrained, Metal ...	Shoulder Joint Metal/Metal Or Metal/Poly...	888.3640	3
KWS	Prosthesis, Shoulder, Semi-Constrained, ...	Shoulder Joint Metal/Polymer Semi-Constr...	888.3660	2
KWT	Prosthesis, Shoulder, Non-Constrained, M ...	Shoulder Joint Metal/Polymer Non-Constra...	888.3650	2
KYM	Metallic Cemented Glenoid Hemi-Shoulder ...	Shoulder Joint Glenoid (Hemi-Shoulder) M...	888.3680	3
MBF	Prosthesis, Shoulder, Semi-Constrained, ...	Shoulder Joint Metal/Polymer/Metal Nonco...	888.3670	2
MJT	Prosthesis, Shoulder, Humeral (Bipolar Hemi-Shoulder) Metal/Polymer, Cemented Or Uncemented			3
PAE	Upper Extremity Prosthesis With Multiple ...	Upper Extremity Prosthesis Including A S...	890.3450	2
PAO	Prosthesis, Shoulder, Semi-Constrained, ...	Shoulder Joint Metal/Polymer Semi-Constr...	888.3660	2
PHX	Shoulder Prosthesis, Reverse Configurati ...	Shoulder Joint Metal/Polymer Semi-Constr...	888.3660	2

以MAUDE進行檢索

- 網址: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm
- 在Product Code 欄輸入關鍵字，例：LPL (soft contact lenses)



用於評價適用性的樣評估標準

適用性要求/標準	描述	評分系統	
合適的器材	評估中器材的資料是從何產出的?	D1 D2 D3	實際上的器材 相等的器材 其他器材
合適的器材應用	該器材是否用在相同的預期使用目的(例如配置方法、應用，等等)	A1 A2 A3	相同使用 微小差異 明顯差異
合適的病患族群	資料由預期治療族群(例如年紀；性別等)以及臨床狀況(也就是疾病，包括狀態與嚴重度)具代表性病患族群的何處產出?	P1 P2 P3	適合 局部/受限 不同族群
可接受的報告/資料整理	報告或資料整理是否包含否包含足夠的資訊以進行合理和客觀的評估?	R1 R2 R3	高品質 微小差異 不充足的資訊

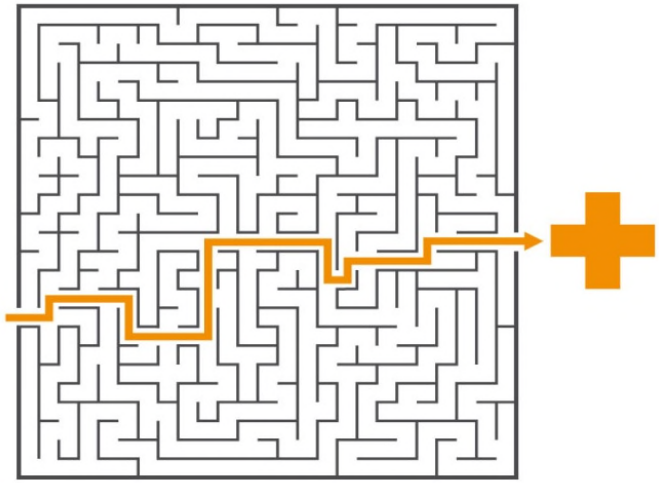
用於評價資料貢獻度的樣本評鑑標準

資料貢獻度標準	描述	評分系統	
資料來源型態	此研究設計是否合適?	T1 T2	是 否
成效指標	此報告中的成效指標是否反應該器材的預期使用性能?	O1 O2	是 否
後續追蹤	後續追蹤持續期間是否足夠用來評估療效的持續以及併發症的鑑別?	F1 F2	是 否
統計顯著性	是否提供資料的統計分析，並且合適?	S1 S2	是 否
臨床顯著性	療效的強度在臨床上的觀察是否顯著?	C1 C2	是 否

課堂練習: 臨床評估文獻搜尋

- 請每位學員與所屬組員討論，嘗試回答演練中的所有問題。

  根據組別，與全班分享您的答案和想法。



Q &A