"Business case" on implementation of TDM in hospital

António Melo Gouveia

Hospital Pharmacist,

Instituto Português de Oncologia de Lisboa de Francisco Gentil, Portugal

Disclosure

Conflict of Interest: Nothing to Disclose

Disclosure

I am NOT:

- An expert in Pharmacokinetics
- A top management specialist

I AM

- Hospital Pharmacist - Chief Pharmacist
- Someone who has to deal with hospital management, medical directors, chief nurses… and pharmacy staff.

Where do I come from

PORTUGAL

- Foundation in 1143 AD
- Population 10 Million
- Language: Portuguese
- EU member since 1986

Where do I come from

Azores

Lisboa

Big Waves small surfer in Nazaré, West Coast

Instituto Português de Oncologia de Lisboa de Francisco Gentil, Portugal

Summary

How to plan, develop and provide TDM service

- Comments on hospital settings - where resources usually go.
- Comments on TDM – Why and How
- Concepts about a Business Plan
- Example of a Business Plan and How it Really Happened (TDM for Bussulfan in BMT)
- Think about your own business plan – a pratical exercise.
- Conclusions

Comments on hospital settings - where resources usually go.

- Fact #1: hospitals in the EU spend a lot of money (in my hospital 110M€/Y)
- Fact #2: Resources go mostly to staff wages and … drugs (50M€/Y)
- Fact #3: despite all talk …
  - drugs that are almost worthless and very expensive are still bought by hospitals.
  - Money is often ill spent in devices which are not fully used, in software that works well in a slideshow, etc.

Comments on hospital settings - where resources usually go.

WHY ?

Comments on hospital settings - where resources usually go.

BECAUSE

- Fact #1: People value healthcare, so they pay a lot for it.
- Fact #2: Healthcare is based on specialist staff who diagnose and treat disease
- Fact #3:
  - People who sell drugs and other stuff are key drivers of spending
  - It's called "marketing", and big pharma is very good at it.

Comments on hospital settings - Healthcare staff.

Physician:

- Has practical based learning (working with senior doctors, learning how to decide)
- Has a huge responsibility: to decide what is happening to the patient and how to cure it, based on little information

Pharmacist:

- More scientific based learning.
- Trained for doing things, has to find a way to people ...

Comments on TDM – **Why** and How

- There is a NEED!
  - Peoples live's are at stake, they just don't know about it.
- There is a WILL!
  - Commited pharmacists know this is important, and have the basic knowledge to do it.
  - They are ready to learn more (improve competencies) and put it to work
- There is a WAY!
  - Just channel a tiny part of the hospital resources for this …

Comments on TDM – Why and **How**

- Show people the need!
  - It´s all about marketing a new service.
  - The added value is there, just show it.
- Improve the Pharmacist:
  - Improve knowledge, show that you can do it better.
  - Be always ready, TDM is not something you do when it is convenient for you. It's when it's needed that matters!
- Added value can be turned into money:
  - find ways to make calculations, this money is needed for extra staff hours and software:
    - » What's the cost of the next antibiotic?
    - » What's the cost of defibrotide?
    - » What's the cost of life?????

Comments on TDM – By the way…

- Clinic
  - Kinetic
    - Genomic

The Path from Life to Science…

Not the Other Way Around

Concepts about a Business Plan

- A **business plan** is a formal statement of:
  - business goals
  - reasons they are attainable
  - plans for reaching them

  (Wikipedia, 05/10/2018)

  If you use a browser, you can find details on how to make a business plan, for instance: https://articles.bplans.com/how-to-write-a-business-plan/

A Business Plan for **TDM**

Keep it short: if it's too big, nobody will read it. "They" don't know what is TDM, don't make it harder.

Know your audience: "They" are:

- Patients? No, they don't decide about this.
- Doctors? Definitely! They can be your allies and make it work, or your worst enemies and make it fail. After all, you're advising them…
- Nurses? Of course, blood samples at the right moment will not happen on their own. They have more work because of TDM
- Hospital managers: they decide on the money …

A Business Plan for **TDM**

Know your audience: "They" need to understand what you say…

- **Don't say** "Drug quantification will be done using LC-MS/MS technology. The PK analysis will be done using a 1-compartment model. The interpatient coefficient of variation (CV) in drug clearance significantly decreased from 60% (covariate-free model) to 30% (BW covariate model). There was a clear improvement in the accuracy to achieve the target AUC over time, with a change from 75,7 mg * h / L on the 1st day (prior to TDM) to 11,6 mg * h / L on day 4. 83% of patients had an optimal exposure to the drug (AUC target value ± 10%). This is likely to allow for decreased risk of toxicities, such as aGVHD) and VOD"

A Business Plan for **TDM**

- **Say:** “If we take blood samples from the patient, do some specific analysis and then allow the pharmacist to use specific software and provide advice, you can reduce side effects of drug X and reduce cost on care and subsequent, more expensive drugs.”

A Business Plan for **TDM**

Don’t be intimidated.

- Your proposal is about improving the lives of patients. You know you can do so much with so little plus your knowledge. You’re not seeking undue advantage. You’re strong because you’re right.
- Go for alliances. It shouldn’t be you vs management asking for more resources. It’s should be doctors asking for your service and …

A Business Plan for **TDM**

Executive summary

- The overview: what you want to do, how do you plan to do it. NMT 2 pages.

Opportunity

- This section answers these questions: What do you really want to do and how are you solving a problem (or “need”) for your “market”? Who is your target “market” and “competition”?

A Business Plan for **TDM**

Opportunity: the Bussulfan Example

What I want to do:

- I want to find bussulfan concentration in blood and use this information to improve dosing and reduce serious side effects.

A Business Plan for **TDM**

Opportunity: the Bussulfan Example

Is there a Problem?

- The problem is that bussulfan is very toxic in the doses used for Bone Marrow Transplant, and every patient metabolizes in it's own way, so standard dosing is not a good option. We had some cases of Veno Occlusive Disease (VOD), some patients died and we spent about 70 000€ in each one of them just with defibrotide (plus ICU, etc.).
- This is NOT a pharmacy thing: many big centers for BMT do this, and the doctors really want it (it was their idea in the first place).

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Execution

- How am I going to do it and how to a measure my results?
- Bussulfan is not an easy drug:
  - No analytical “kits” in the market (immunoassay)
  - Not easy to dose with HPLC-UV; Derivation chemistry is not a real option, implies loss of precision and time.
  - Time is fundamental: you’re adjusting doses in real patients, who undergo a four day regimen.

A Business Plan for **TDM**

Execution

- You need to do HPLC-MS but … you don't have this in the hospital and there is no nearby center ready to sell this expensive test. Time is crucial.
  - We found a partner in the National Institute for Legal Medicine (forensics lab). They are ready to receive a sample by 8AM and provide a result by 2 PM. (300€/patient)

A Business Plan for **TDM**

Execution

- You need knowledge on the analytics and on turning data into dose recommendations, and someone who can validate ours results.
  - The Faculty of Pharmacy of Lisbon is our partner in development and methods for turning data into doses.
  - The UMC Utrecht was a huge support in knowledge and advice on analytics and data analysis.

A Business Plan for **TDM**

Execution

- Knowledge for the hospital pharmacists – you'll be suggesting dose changes of 50% - life or death in the balance!
  - The Faculty of Pharmacy of Lisbon provides strong knowledge support (their return may be in the form of published papers)
  - Trust in the analytics of the legal medicine people, validation and cross validation of methods.
  - The UMC Utrecht again a huge support.

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Execution - Workflow:

- Blood samples at the right moments, from 6PM to midnight. **Nursing staff is involved.**
- First treatment of blood samples plus freezing: immunohemotherapy service is involved.
- Sample transport by a contractor, picks up at 7.30AM in the hospital, delivers by 8.00AM at legal medicine.

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Execution - Workflow:

- Legal medicine runs samples and delivers results by 2PM.
- 2 parallel validated HPLC-MS systems. Availability schedule known in advance and is part of BMT scheduling (doctors involved)
- Pharmacy runs results in software (ADAPT – 5), dose suggestions are double checked by pharmacists and dose change suggested before start of second day of treatment (6PM)

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Execution – General Thoughts:

- Access to patient data is mandatory. As a minimum, lab results, but it should be the patient clinical record.
- Get information to physician:
  - Paper ???
  - E-mail ???
  - Write in the patient clinical record!
  - Use the prescription software

A Business Plan for **TDM**

The Team and the Hospital Pharmacy

- Hospital pharmacists have a good reputation for reliability - You have also to sell this to your staff, they will be afraid to suggest dose changes where life is in the balance.
- Rest of the team: Faculty of Pharmacy, Legal Medicine, involvement of doctors, nurses, immunohemotherapy, support from reference center (UMC Utrecht) – What a great team!
- No need to hire new staff now, we can show results and discuss later …

A Business Plan for **TDM**

Financial plan

- Staff: just additional effort and new tasks
- Analytics: 300€/patient (3 days).
- Software: proprietary (?), maybe 12000€/Y

Cost of NOT doing it (besides life):

- Each VOD patient:
  - 70 000€ in defibrotide
  - ICU costs
- Have to do 4 doses/day instead of one (nursing staff)

A Business Plan for **TDM**

Financial plan

- Prepare from the start the study to show your results:
  - Before and after
  - RCT
  - Whatever…
- In the end, you should commit to show that your results are a good investment.

A Business Plan for **TDM**

Appendix

- Details
- Charts
- Tables

- Everything they need to feel safe on the rightness of the decision to support the project.

By the way … did it work?

- We implemented TDM for bussulfan in BMT. From initial steps to routine TDM 2 years went by. Patient PK variability was assessed and TDM efficacy is being assessed. Side product was a master thesis (http://repositorio.ul.pt/handle/10451/28434). More publishing in the future.
- 3 steps:
  - Literature search, consult with reference centres and research labs for analytics. Development and validation of analytics by LC-MS in the forensics lab of the National Institute for Legal Medicine. Development on PK analysis using ADAPT-5 software.
  - Pilot: doing a feasibility check of procedures, cross validation of results with UMC Utrecht
  - Implementation: put procedure in clinical routine, with daily dose adjustment. Prospective observational study with clinical and pharmacokinetic data. Dosing schedule already changed for 4 daily to 1 daily.

By the way … did it work?

Results:

- It started mid 2014- By the end of 2017, 21 patients involved.
- Optimal exposure to the drug increased from 42 to 83%.
- Doses were reduced (up to 37%) in 10 patients, and increased in 3 patients (up to 19%).
- Prospective study to get clinical data is ongoing,
- From pharmacy manager point of view, defibrotide expenditure fell more than 140 000€, only one patient treated for suspected VOD didn't have TDM …

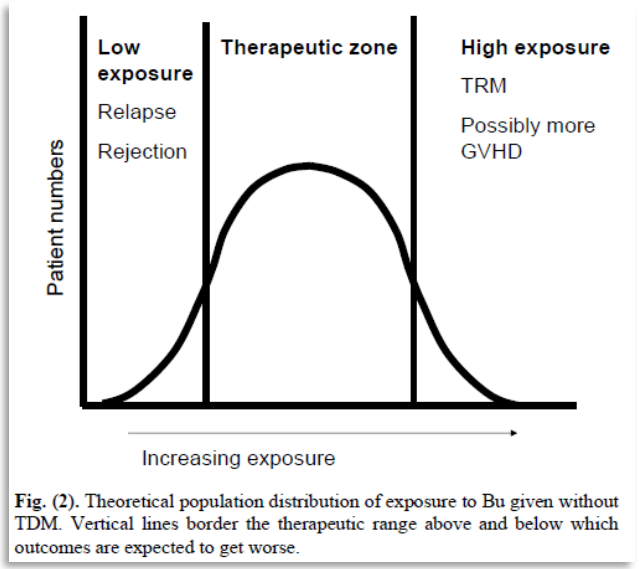

Fig. (2). Theoretical population distribution of exposure to Bu given without TDM. Vertical lines border the therapeutic range above and below which outcomes are expected to get worse.

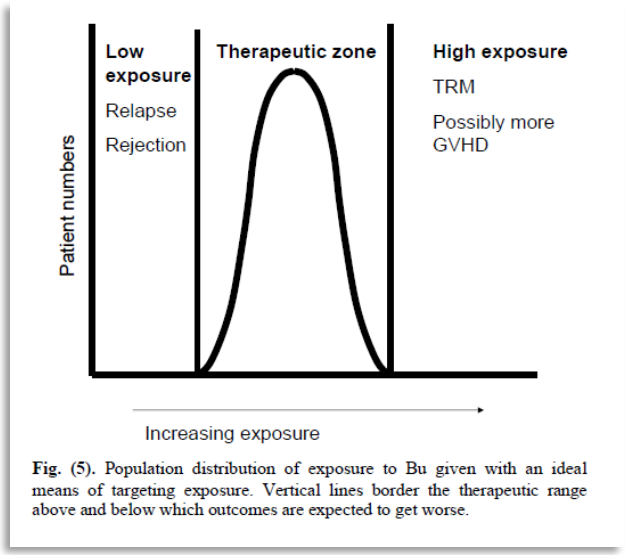

Fig. (5). Population distribution of exposure to Bu given with an ideal means of targeting exposure. Vertical lines border the therapeutic range above and below which outcomes are expected to get worse.

Warsaw 2018

J.A. Russell et al. Current Pharmaceutical Design, 2008, 14, 1936-1949

Your Business Plan for TDM

- Opportunity: why do it?
- Execution: how to do it?
- The Team: who will do it?
- Financial Plan: How is it paid?

Your Turn Now!

Focus on the Patient

- In the decision making process...

THINK!

WHAT IS BETTER FOR THE PATIENT?

Conclusion

- Resources are there, just find a way to get a tiny part of it!
- TDM is good value for money – it's not expensive (as compared to drugs) and provides results. Just sell it.
- A Business Plan is just a way to do this, there are many others, the important thing is to do it.

We Can Always Change for the Better!

Thank You for Your Attention