

Expert Forum

The Fifth New Zealand Treat-to-Target
in Rheumatoid Arthritis National Meeting



Making Education Easy

14 & 15 October 2016

Agenda items

➤ **An introduction to Treat to Target: progress in New Zealand, future aims**

- Assoc Prof Andrew Harrison

➤ **Setting out to achieve targets and goals: Practical application of T2T in RA**

- Assoc Prof Simon Stebbings

➤ **Delivering T2T in a resource-constrained environment: Encouraging high quality referrals**

- Dr Doug White

➤ **Delivering T2T in a resource-constrained environment: Working with our GP colleagues**

- Dr David Porter

➤ **Keeping our patients at the centre of Treat to Target in NZ: Hearing secret harmonies**

- Assoc Prof Andrew Harrison,
PORTAL Participant

➤ **Keeping our patients at the centre of Treat to Target in NZ: Empowering the patient to measure their targets**

- Dr Rebecca Grainger

➤ **Keeping our patients at the centre of Treat to Target in NZ: A tailored approach to empowering the patient**

- Dr Doug White

➤ **Debate: "The toolbox is full – we already have what we need to treat RA to target"**

➤ **Imaging and Treat to Target**

- Assoc Prof Fred Joshua

➤ **Future directions for T2T: What do we do with the stable patient?**

- Assoc Prof Fred Joshua

➤ **Workshop: Beyond DAS28 remission for Kiwi RA patients**

➤ **Nurses' Breakout Session: Treat to Target – Enhancing the role of the Rheumatology nurse**

- Dr Mike Corkill

Welcome to this review of the Fifth National Rheumatology 2016 Treat-to-Target (T2T) Meeting, held in Wellington.

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The theme for the 2016 T2T Meeting was *Treat to Target through time: Where have we been and where could we go?* Associate Professor Andrew Harrison (T2T Ambassador) welcomed attendees and thanked AbbVie New Zealand Ltd for their sponsorship of T2T and TUI, and for facilitating and sponsoring attendance at both meetings. The meeting audience included rheumatologists, rheumatology nurses and patients, as well as representatives from Arthritis New Zealand and AbbVie.

The first session of the 2016 T2T Meeting reflected on progress made in New Zealand and described future aims of T2T. Presentations described the practical application of T2T in RA, its delivery in a resource-constrained environment, and working with GP colleagues to ensure the best outcomes for RA patients.

Session Two reported on the Portal Project, patient-reported outcomes with an app designed to empower patients to measure their treatment targets, and discussed data from an NZ project that has placed RA patients at the centre of their own care. A light-hearted debate discussed whether or not clinicians need to go further in terms of treating RA to target.

The third session began with presentations concerning ultrasound imaging and T2T, and consideration of future directions for T2T, including the possibility of treatment tapering in stable RA disease. Data are reported from a workshop that explored outcome measures and disease targets that are meaningful for patients. The last item in the T2T agenda was a workshop that discussed how to enhance the nurse's role in assessment of RA patients.



Andrew Harrison's
Introduction to
T2T 2016

FRIDAY 14 OCTOBER 2016
SESSION ONE – CHAIR: ANDREW HARRISON

T2T in New Zealand, progress to date and future aims

– Assoc Prof Andrew Harrison (T2T Ambassador)

Treat-to-Target is a global initiative that seeks to optimise outcomes in rheumatoid arthritis (RA) through tight control of inflammatory disease and treating RA to target, using an evidence-based approach. Based on the evidence, a Task Force identified 4 overarching principles and 10 specific recommendations for treating RA to target, defined ideally as remission of clinical disease activity.

Treat-to-target has been funded internationally by AbbVie and locally by AbbVie New Zealand. The New Zealand T2T Steering Committee* was formed in 2010.

The inaugural national T2T Meeting in October 2010 hosted a panel discussion, explained the treatment recommendations, discussed the results of the NZ T2T Physicians' Survey, evidence from case studies, treatment targets and composite indices. The meeting also held a joint calibration workshop and ultrasound workshop.

The second national T2T meeting in December 2011 was organised around the theme: *Delivering T2T in a resource-constrained environment*.

The theme for the third national T2T meeting in August 2013 was *Collaborating with primary care to optimise service delivery and patient outcomes*.

The fourth national T2T Meeting in March 2015 was themed: *Patient representation facilitating the participation of the central stakeholder*. It discussed health literacy and shared decision-making, and presented New Zealand survey data on patient satisfaction.

The 2016 T2T Meeting centred around the achievements that have been accomplished in New Zealand since the inaugural meeting. Outcomes of a joint examination workshop have been published in *The Journal of Rheumatology*,¹ a joint examination video presented at the International T2T Meeting in Berlin in 2012 is available on YouTube, and the GPSI (general practitioner with a special interest) training module is being used and has assisted the formation of a PHO-funded rheumatology service in the Nelson region. Furthermore, an online patient portal has been developed by a group of rheumatologists, as a means of gaining access to patient opinion.

*Assoc. Prof. Andrew Harrison (Chairman), Dr Michael Corkill, Sandra Kirby, Assoc. Prof. Simon Stebbings, Dr Douglas White



Setting out to achieve targets and goals: Practical application of T2T in RA

– Assoc Prof Simon Stebbings

The objectives of T2T are to:

- Drive timely treatment decisions for optimal patient outcomes
- Better engage patients as partners in the management of their condition
- Define a new, internationally accepted standard of care for RA
- Improve access to treatments and resources, where needed and possible

T2T for rheumatologists:

- Presents relevant clinical evidence to provide an evidence-based daily practice goal for rheumatologists
- Guides and homogenises clinical decision-making within and across countries
- Clear outcome targets and tight disease control should be integrated into standard practice

T2T for patients:

Involving patients is considered to be vital, to help them understand the importance of disease control and empower them to reach decisions regarding their disease management in partnership with their rheumatologist and other health professionals.

The 10 recommendations on treating RA to target are divided by subject matter:

- Recommendations 1–3 concern the achievement of low disease activity, or remission, and controlling the inflammatory process
- 4–5 concern the frequency of the patient review process
- 6–7 involve the use of validated measures of disease activity demonstrating treatment response
- 8–9 are to do with retaining disease remission and taking into account comorbidities, patients factors and drug-related risks, when choosing disease activity measurement and level of T2T value
- Recommendation 10 emphasises that the patient must be informed about the treatment strategy and supervised by the rheumatologist

Clinical evidence from strategy trials and treatment target studies suggests that tight disease control improves outcomes. Polling results revealed that 23% of the audience always and 42% often treat their RA patients to target according to the recommendations; 26% do sometimes and ~8% do rarely. Thus, around one-third are not following T2T guidelines.

Barriers to T2T implementation for rheumatologists

Scant data exist as to why some rheumatologists fail to adhere to the T2T guidelines. Local data indicate that one of the criticisms of T2T data concerns the fact that most of it is research-based, not 'real world'. Also, most outcomes are based on a rigid escalation of therapy according to a set protocol, versus a real-world clinic environment.

A recent paper questioned whether T2T in RA is fact, fiction, or hypothesis.² It pointed out that all patients are not the same, so treatment strategies may not be effective for all, and rigid treatment targets may not be relevant in real, everyday practice. It questioned whether T2T does indeed reduce damage, disability and mortality. Moreover, adding more drugs to the patient's treatment regime may lead to higher rates of drug toxicity and drug-induced damage. The article also asked whether patients are true partners in the process and understand the concept of T2T, and how their choices of treatment affect the control of their disease.

A survey conducted in primary care identified perceived barriers to guideline adherence:

- knowledge-related barriers (lack of awareness/familiarity)
- attitude-related barriers (e.g. lack of agreement, inertia of previous practice/lack of motivation)
- external factors (the clinician may not reconcile patient preferences and demands with guideline recommendations, or may believe guideline recommendations are unclear or ambiguous, incomplete, or too complex, or may face lack of time/time pressure, lack of resources/materials, or organisational constraints within the department/clinic or required liaison, such as physio access).³

An Australian investigation identified clinical situations in which rheumatologists elected to continue RA patients with moderate disease activity (MDA) or high disease activity (HDA) on DMARD therapy without adjustment to achieve clinical remission or a low disease activity (LDA) target of a DAS28-ESR score <3.2.⁴ The most commonly identified barriers to achieving tight control in RA included longstanding disease with irreversible joint damage, patient- and rheumatologist-driven undertreatment, noninflammatory musculoskeletal pain, and insufficient time to assess response to recently initiated DMARD.

An audience poll revealed that resource constraints in the public health environment represent the biggest barrier in treating RA to target.

In 2012, a retrospective audit of Dunedin's public hospital rheumatologists assessed their adherence to T2T recommendations. Electronic case reports from 124 RA patients (mean age 59 years; 74.2% females) attending 5 consultant rheumatologists were assessed from a 6-week period (March to mid-April 2012). The majority of patients were seropositive (93.5%).

- Recommendation 6 of the T2T treatment recommendations advises that a validated composite measure of disease activity (e.g. DAS28) should guide treatment decisions. The audit revealed that fewer than half (43.5%; n=54) of the patients had a DAS28 score. However, the mean DAS28 score was 2.61 (range 0.96 to 6.7), indicating that patients were being kept close to remission; mean DAS28 scores did not differ by consultant (F=2.65; p=0.059). Of the 70 patients without a DAS28, 11 underwent a qualitative assessment (gestalt impressions) only; 6 had active disease and 5 inactive disease. Of the active disease cohort, treatment was adjusted in 2 patients and unadjusted in the remaining 4.
- Recommendation 3 advises that remission is a clear target and LDA is an acceptable alternative goal, particularly in longstanding disease. Of the 23/54 (43%) patients with a DAS28 score >2.6, treatment was adjusted in 12 and not adjusted in 11. Reasons for not adjusting treatment in active disease patient choice (n=1), comorbidities (n=1), uncertainty (n=8), and inactive status (n=1).
- Recommendation 5 advises regular follow-up of patients and that when treatment is adjusted, patients should be checked for sustained LDA or remission. In this audit, 39.2% of patients were seen at 3 months' follow-up, 57.5% at 4 months and 90% at 6 months. The mean follow-up time was 4 months for patients with active disease (DAS28 >2.6) and 6 months for those with inactive disease (DAS28 ≤2.6).
- Recommendation 7 advises that structural changes (X-ray) and functional impairment (HAQ) should also be considered when making clinical decisions. HAQ score was not recorded in any of the electronic files. Annual follow-up X-ray data was available for 122 patients; an annual X-ray was completed in 42.6% of this cohort.

The audit revealed inadequate implementation of the T2T guidelines by Dunedin rheumatologists. Further research could investigate why this is the case and how Dunedin compares with other centres.

Delivering T2T in a resource-constrained environment: Encouraging high quality referrals

– Dr Doug White

In December 2012, a survey conducted by Dr White in his Hamilton practice revealed differences amongst his colleagues as to triage decisions of referrals. This was partly due to the lack of information in the referrals limiting fully informed decision-making. It was also due to the cumbersome hospital process at the time.

Determining access to rheumatology services

Dr White and colleagues have devised a multidimensional framework for determining access to rheumatology services, which initially requires GPs to score their RA patients before referring the patients to hospital.⁵ The referral centre now sends the data electronically to the rheumatologists, who determine whether rheumatology first specialist assessment is appropriate for these patients. If it is, the referral is checked for red flags (e.g. presence of acute vasculitis, giant-cell arteritis) and whether the service can provide access for the patient (this decision depends upon the scoring system), after which a level of urgency is assigned to the case. Implementing this framework has improved the turnaround time for all referrals from a mean 7 days to just 1 day. Patients are receiving better care, within local resources. An evaluation of this scoring system will be published in the future.

Results of this project won an award for healthcare improvement excellence at the APAC Forum in 2015, an Asia Pacific health care conference managed by Ko Awatea, the centre for health system innovation and improvement at Auckland's Counties Manukau Health. The framework can be adapted easily by different health care services and has enabled the development of a primary care pathway.

Project outcomes

The implementation of this project has enhanced appreciation of team members' skills and strengthened the team's interaction with primary care.



Delivering T2T in a resource-constrained environment: Working with our GP colleagues

– Dr David Porter

Typically, rheumatology patients need repeated follow-up for resolution of disease- and/or medication-related issues that differ from appointment to appointment such as disease flare and infectious complications; they are not on a linear path of disease improvement. Discharge of these patients is near-impossible and thus, funding criteria need to plan for ongoing follow-up of a large proportion of patients. The Nelson PHO has recently announced a 50% increase in funding for ongoing follow-up of rheumatology patients, which should help with the workload and shorten the time between appointments.

Build in redundancy?

In mid-2013, Dr Porter entered into a collaboration with the Nelson PHO, which established funding for his involvement in a once-weekly clinic that involves GPs and rheumatology nurses. Once a month, he attends an all-day clinic in Waiau, serving as a Consultant for rheumatology treatment advice. Although the concept is sound, there are resourcing problems. Dr Porter suggests that building redundancy into the health system would be useful. Having a pool of 5 GPs for a once-weekly rheumatology clinic would overcome the situation of only ever having 3 GPs dedicated to the clinic and the associated problems that arise when one or more of the GPs is unable to be in the clinic on the day. Moreover, having a back-up Consultant would provide support for those occasions when Dr Porter cannot attend the clinic.

SESSION TWO – CHAIR: ANDREW HARRISON

Keeping our patients at the centre of Treat to Target in NZ: Hearing secret harmonies

– Assoc Prof Andrew Harrison (with PORTAL Participant)

In 2014, Assoc Prof Harrison and colleagues* set up the Rheumatoid Arthritis Patient PORTAL (Patient Opinion Real-Time Anonymous Liaison) project, to enable sampling of patient opinion about treatment and explore what they perceive to be important in their RA care. At the 2015 national T2T Meeting, the PORTAL members agreed that this project would also provide the means to keep patients at the centre of T2T. No other such initiative exists internationally.

PORTAL surveys

RA patients were recruited from rheumatology clinics in Hamilton, Wellington and Dunedin, and via the Arthritis New Zealand website. Approximately 140 patients are currently participating in PORTAL. Their participation in online surveys has helped to inform the design of a range of questions; those patients unable to access the internet have been approached by telephone survey.

Responses from the first PORTAL survey revealed that 85% of patients strongly agreed or agreed with the second statement “*I worry about how my arthritis will affect me long-term*”. Seeking to determine what patients worry about, the PORTAL Committee then constructed more statements, including: “*I worry about how my arthritis will result in erosions in my joints*”. Approximately 83% of patients agreed with this statement. They also worry about long-term effects of medications; a similarly high proportion of patients believed that medications can cause long-term problems. Disability was apparently not as great a concern as erosion. A lot of concern was expressed around the statement “*I worry that my arthritis will affect my capacity to take part in aspects of life such as employment, recreation and family activities*”. Much less concern surrounded the statement: “*I worry that my arthritis will affect my life expectancy*”.

Data were collected from the first 60 PORTAL participants in the original survey, then the same survey was sent out to a second cohort of 60 patients, to determine whether the rolling recruitment process would influence patients' opinions. There was no evidence of an effect; the proportions returned were not statistically different from the first lot of data. It was decided that PORTAL could enrol patients as they became available, without adverse effect on patients' opinions.

The Committee designed two surveys to elicit patients' opinions on T2T. The first survey concerned the overarching principles; the second involved the 10 recommendations. Subsequent surveys explored areas of interest that emerged from the responses.

- A very high level of agreement was expressed (close to 100% for some items) with all of the overarching principles, with shared treatment decision, and there was almost universal agreement with the notion that symptom control, prevention of structural damage and social and functional participation is a primary treatment goal. Abrogation of inflammation was seen as an important way of achieving these goals.
- As for the treatment recommendations, there was strong agreement with a state of clinical remission, but a lower level of agreement with the notion that it was acceptable to use LDA as an alternative target. The level of agreement was relatively low for the statement “*Until the desired target is achieved, therapy*

should be adjusted at least every 3 months”. There was 100% agreement with the notion that the rheumatologist should involve the patient in setting the treatment strategy to reach this target. Pairwise comparisons revealed no significant differences in levels of agreement between statements 1 and 2, but there was strong and equal agreement that the target should be clinical remission and should be defined as the absence of signs of inflammatory disease; there was significantly less agreement that LDA was an alternative target. The level of agreement with Recommendation 8 (that treatment should be adjusted every 3 months) was significantly lower than all of the remaining 9 recommendations.

- The PORTAL Committee examined patients' free text comments, to determine whether they considered 3-monthly adjustment of treatment to be too frequent or too infrequent. Of 22 patients who commented on interval, only 1 stated that 3 months was too long; 9 considered 3 months to be acceptable; 10 responded that 3 months was too short (because drug therapy could take up to 6 months to be effective).
- A subsequent survey considered the high level of agreement with Recommendation 10 (that the rheumatologist should involve the patient in treatment decisions) and asked a question concerning skills and communication; the relative value placed on abrogating inflammation versus maintaining quality of life; and patients' perception of the validity of rheumatologists' measures of disease control.

Patients expressed a high level of agreement with the statement: “*My rheumatologist has the expertise and experience to decide on the best treatment for me; my opinion should be taken into account, but the decisions should be made under the guidance of my rheumatologist*”.

- Survey 4 explored the low level of agreement with the statement: “*The method that rheumatologists use to measure inflammation, e.g. counting tender and swollen joints, testing for CRP, give a good reflection of how arthritis is controlled*”. Surprisingly, X-ray evidence of erosions ranked the highest; fatigue ranked the lowest. Fatigue and CRP levels ranked significantly lower than ultrasound evidence of erosions and inflammation. Health-related QoL, MR evidence of erosions, and pain ranked highly with patients.

* Merrin Rutherford (5th year medical student), Sandra Kirby (Arthritis New Zealand), Assoc Prof Simon Stebbings, Dr Doug White

In conclusion

The polling revealed a high level of patient agreement with the principles; LDA is less acceptable as a target; a relatively lower level of agreement with the need for 3-monthly review; unanimous agreement with the need to involve patients in decision-making; a greater agreement with rheumatologists taking the lead versus patients taking the lead; DAS28 inputs were in the lower part of the outcome measures as ranked by agreement; erosions, pain, health-related QoL, and ability to cope were regarded as better indicators of worsening arthritis than CRP.

The poll has obtained data on the demographics of an unselected group of RA patients and has proven to be an effective means of obtaining patient opinion on T2T. This method has a range of applications. Planned improvements include automated standardisation of the data against the general RA population.



Future uses for PORTAL

The Committee has entered into a trans-Tasman collaboration on T2T with Dr Helen Benham (Diamantina Institute, Brisbane) and is in talks with the Rheumatology Guidelines Group on the revision of the APLAR guidelines; patient input will be sought from PORTAL users, for contribution to the guidelines. A review of PORTAL services is scheduled to be held in Wellington. The Committee is extremely grateful to AbbVie for their unrestricted support of the project, to Arthritis New Zealand for use of their website for patient recruitment, and to the patients who are contributing to PORTAL.

Keeping our patients at the centre of Treat to Target in NZ: Empowering the patient to measure their targets

– Dr Rebecca Grainger

The definition of patient-centred care has changed over time. In 2001, the Institute of Medicine defined patient-centred care as “providing care that is respectful of, and responsive to, individual patient preferences, needs and values, and ensuring that all patient values guide all clinical decisions”. The failure of this definition to embrace the wider system that the patient is embedded within is addressed by a revised definition; “*the experience (to the extent the informed, individual patient desires it) of transparency, individualization, recognition, respect, dignity, and choice in all matters, without exception, related to one’s person, circumstances, and relationships in health care*”.⁶ Does our health care system embrace all aspects of this definition of patient-centred care?

Arguably, rheumatology practice expresses important aspects of patient-centred care, involving choice of the right medication for the patient at the right time, with continuity of care. The overarching principles guiding T2T sit within a model of patient-centred care, although the stipulation that patients be seen every 3–6 months does account for the variability of disease between patients.

A patient-held app for RA

Dr Grainger and colleagues have developed a concept for patient-led management of RA – a smartphone app that records disease activity metrics. In the future, this could be enabled to communicate the data to the rheumatology care team. The disease activity data could then be used to rationalise appointments and consult health care professionals when needed, rather than according to a prescribed timetable. The app, “RACoNnect”, collects some of the data normally recorded in the clinic: Patient Global, Patient Pain, and the 10-item HAQ2 (see Fig. 1).

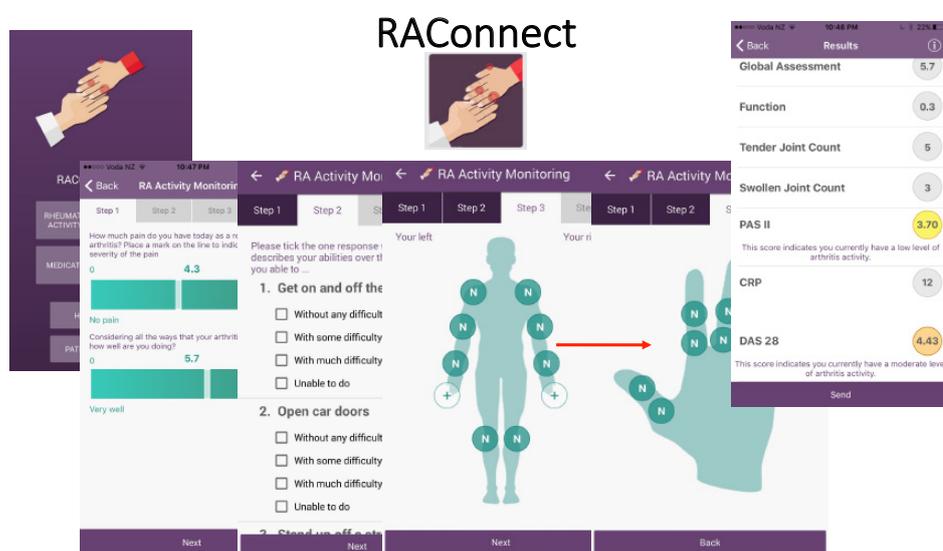


Figure 1. Title screen of RACoNnect.

RACoNnect involves patients in their own health care

Within RACoNnect, people with RA enter their own joint count on a homunculus. Results are expressed after patients complete their input. These data could be used as part of the implementation of T2T. Currently, people with RA can send their completed record to an email address of their choice; it is intended that the app will send the data directly to a hospital-based clinical data repository, for display on Concerto. This means the patient-reported RA disease activity data could be tracked over time.

Some healthcare professionals have expressed concern over RA patients conducting their own joint count evaluations. Would training enable patients to produce joint counts that align closely with those of their healthcare professionals? Dr Grainger and colleagues plan to investigate this in a workshop involving patients with RA and rheumatologists. The outcomes of this workshop will be used to develop videos for online viewing for train patients with RA to conduct their own joint counts. The impact of this video will be assessed in patients presenting to rheumatology outpatient clinics in 2017. This project can be described as an extension of T2T – involving patients in their own health care.

Dr Grainger thanked AbbVie for their unrestricted grant enabling the development of RA Connect.

Keeping our patients at the centre of Treat to Target in NZ: A tailored approach to empowering the patient

– Dr Doug White

A key concept behind the implementation of T2T is how to effectively communicate with patients, and how to deliver appropriate information to them in a way that they can best understand. The behavioural concept of patient activation plays an important role in this communication delivery. By linking knowledge, skills and confidence, behavioural activation leads to empowering behaviours that help people to engage better with health care.

The PAM concept

The Patient Activation Measure® (PAM) was developed in 2004 to assess patient knowledge, skill and confidence for self-management.⁷ This patient-reported measure has been validated in the UK and has proven to be a powerful and reliable measure of patient activation in many disease areas, including rheumatology.

Patient activation scores lie on a scale of 0 to 100 and are often subdivided into four groups, known as ‘levels of activation’. These range from low to high activation. Evidence in the literature suggests that ~40% of people (including RA patients) are in the lower two groups. Measurement of activation is linked to patients’ engagement with health care utilisation, to outcomes that are important to clinicians such as number of consultations, consultation frequency, as well as satisfaction. The PAM can also monitor the implementation and development of other programmes.

Patient activation is related to engagement in preventive behaviours, treatment and healthy behaviours. People in the lower levels of activation do not engage well with health care services. As people move up through the levels, those who are more activated are significantly more likely to engage in healthy behaviours like eating a healthy diet, or regular exercise. Self-management behaviours improve. In long-term conditions such as HIV and diabetes, more-activated patients are more likely to be adherent to drug regimens, obtain regular care and have better clinical outcomes associated with the condition than less-activated patients.⁸ More-activated patients have lower rates of hospitalisation and fewer visits to A&E departments and health practitioners than less-activated patients.^{9,10} The PAM concept has become an important concept of delivering NHS care in the UK across a number of different areas.

It is hoped that the use of PAM in rheumatology will deliver tailored information at a level that is appropriate to the patients’ activation state and achieve outcomes that are useful in clinical practice; reducing health care utilisation and improving the quality of interaction are important goals. The entire platform is an online resource that is user-friendly and accessible.

In summary

Dr White believes that nurse practitioners and allied health staff will consider this information to be very helpful and a useful framework for interacting with patients. Initially, the PAM scheme is planned to be rolled out in rheumatology clinics in Auckland, Hamilton and Wellington. Depending on uptake and outcome, the platform may be modified and adapted for ongoing use.



SATURDAY 15 OCTOBER 2016
SESSION THREE – CHAIR: ANDREW HARRISON

Imaging and Treat to Target

– Assoc Prof Fred Joshua

Audience polling revealed that the majority of rheumatologists use X-ray and ultrasound (US), and MR at some point; a few use no imaging methods.

Guidelines for T2T describe the goal in RA treatment as maximising long-term health-related QoL through the control of symptoms. Prevention of structural damage is a central tenet in the first guideline. However, without some form of imaging, it is impossible to measure structural damage; the target remains undefined and it is impossible to treat to target.

Inflammation is a measure of disability in the short-term. In the long-term, disability and mortality is best linked to erosive change on X-ray. US and MR joint damage is then linked to X-ray. Preventing joint harm prevents severe functional declines, work disability, and increased mortality.¹¹

Data on imaging as a treatment target

EULAR has published recommendations for imaging in RA:¹²

1. When there is *diagnostic doubt*, conventional radiography (CR), US or MR can be used to improve certainty of diagnosis above clinical criteria.
Imaging can now be used for making a diagnosis and is accepted by the ACR and EULAR guidelines for classification of RA. US and MR evidence is clear about the sensitivity and specificity of inflammatory arthritis, beyond clinical examination. Using MR as the gold standard, a clinical examination will miss synovitis in 3 to 4 patients in every 10; US will detect synovitis in 8 to 9.
2. Inflammation seen on US or MR can be used to *predict progression* to clinical RA from undifferentiated inflammatory arthritis.
Thus, imaging can be used to help determine stratification; determine which patients are of more concern to the rheumatologist.
3. US and MR are *superior to clinical examination* in detecting joint inflammation for more accurate assessment in inflammation.
4. *US and or MR* should be considered if CR does not show damage and may *detect damage at an earlier time point* – especially in early RA.
5. Bone marrow oedema on MR is a strong independent *predictor of subsequent radiographic progression* in early RA and joint inflammation on US. Synovitis on MR or US, and erosions detected by CR, MR or US could be used as prognostic indicators. Thus, imaging helps to guide treatment.
6. Inflammation on imaging may be *more predictive of a therapeutic response* than clinical features.
US and MR can be useful for demonstrating therapeutic response in cases that appear to be resistant to treatment (e.g. residual swelling) and support continuation of treatment, or for demonstrating lack of response and support treatment cessation.
7. US and MR may be useful in monitoring disease activity, as they allow *improved detection of inflammation*.
In a patient with no detectable disease, feels good, blood tests are normal, but MR or US results demonstrate evidence of disease, is action warranted? Two studies conducted in 2016 suggest that there is not much more benefit in treating to complete radiographic remission, because the risk of developing more treatment-related side effects is increased statistically, although the patient may not need much more drug, because the clinical impact may not be enough. The issue with this is that there was a trend towards better radiographic damage over 18–24 months (without statistical significance). In a young person, this extra reduction may make a difference over time, as the disease is long-term and the effect of joint damage is magnified. However, in an elderly patient with minimal joint inflammation, drug therapy may expose the patient to more harm than benefit. This recommendation may change, as more data become available.
8. CR should be considered periodically to evaluate joint damage, *MR (and possibly US)* is more responsive to change in joint damage and can *monitor disease progression*.
Imaging with MR (and possibly US) can speed up therapy changes in response to joint damage, which is imaged earlier than with X-ray.
9. CR (in flexion and neutral) should be used to *monitor instability of the C-spine*, MR should be performed if CR positive or if specific neurological findings.

10. In clinical remission, *MR and US can detect persistent inflammation*.
Evidence from a clinical study conducted in 2016 suggests that this recommendation needs to be interpreted with care. In 2013, the information was that MR and US would predict flare of disease. Retrospective clinical data showed that Doppler signals predict joint damage that occur over time, and that MR and bone oedema predict joint damage. Subsequent clinical trial data have shown that stopping joint damage results in less joint inflammation on imaging, but the level of improvement may not be worth it.

Patient care: Using imaging to escalate therapy

A 42-year-old female was first seen in December 2012 as a second opinion. She had a 10-year history of mild idiopathic thrombocytopenic purpura (ITP), treated initially with IV immunoglobulin, and had received prednisone 5–10 mg for 6 years for inflammatory arthritis. She was RF-positive (464) and anti-CCP-positive (113), and was a smoker (20 years). She had 20 swollen and tender joints, ESR 4, CRP 3, VAS 70, and DAS28 3.2. X-ray and CT in March 2012 showed no evidence of erosions.

RA treatments included weekly methotrexate 25 mg, twice-daily hydroxychloroquine 200 mg, and leflunomide 10 mg/day. One year after initial presentation, the patient felt better, but still had active joints clinically with swelling (10 swollen, 0 tender, VAS 10, ESR 5, DAS28 2.15). X-ray data in December 2013 showed erosive change in hands and feet, but the patient was not keen on more therapy. US data confirmed ongoing erosion, which was discussed with the patient, who then decided to commence TNF inhibitor therapy.

Would more therapy help? In an 18-month clinical study, escalating treatment in such cases resulted in more people achieving remission, but without significant change in joint damage.¹³ The ARCTIC study examined whether an US-guided T2T strategy yields better outcomes over time versus conventional clinical examination in RA management.¹⁴ After 16 and 24 months, equal outcomes were observed with 22% of the US tight control and 19% of the clinical tight control arm achieving clinical remission (DAS28 <2.6; no swollen joints, no X-ray progression). The data are reassuring – clinical examination can achieve good results. Should imaging be used as part of a T2T strategy for diagnosis, treatment response and prognosis?

Future directions for T2T: What do we do with the stable patient?

– Assoc Prof Fred Joshua

If patients are doing well on conventional synthetic DMARDs (csDMARDs) and achieve LDA, should they be left on treatment or can they discontinue, to achieve drug-free remission? In audience polling, 80% of clinicians favoured discontinuing csDMARDs.

Should this also be the case for a stable RA patient on both biologic and csDMARD therapy? Polling indicated that 37.5% favour tapering/discontinuing csDMARDs only, 25% would discontinue both.

The 2014 update of the 2010 T2T recommendations are summarised as:¹⁵

In established RA, stopping biologics leads to very frequent loss of low-disease activity or remission, while dose reduction or spacing of intervals of applications carries less risk of return of active disease. In early disease, the question of successful withdrawal is not yet resolved. Stopping csDMARDs is followed by flares more frequently compared with their continuation. Adherence to therapy has also to be considered since non-adherent patients flare up to four times more frequently than adherent patients.

Withdrawing csDMARDs, stepping-down, tapering therapy

In a review of RCT evidence for tapering csDMARDs, 6 trials using DMARDs and monotherapy withdrawal had good clinical responses.¹⁶ Flares occurred in 17% of patients who continued therapy and in 46% of those who discontinued. Post-flare, restarting the DMARD was usually successful. The clinical experience of Assoc Prof Joshua has been that in those cases where restarting the DMARD was not successful, the patients ended up on a greater drug burden than previously. In the review, 4 RCTs examined step-down DMARD combinations to DMARD monotherapy (follow-up was 2–3 years); LDA achieved on combination DMARDs was maintained on monotherapy.¹⁶



Four observational RCTs of tapering or stopping DMARDs in patients with sustained LDA provided supportive evidence for discontinuing in some patients.

The RETRO study involved 101 patients in clinical remission on ≥ 1 conventional and/or biological DMARDs.¹⁷ Overall, 66% remained in remission for 12 months after stopping or tapering therapy and 33% relapsed. Patients continuing full-dose conventional and/or biologic DMARD did well (16% flared); reducing the dose of all conventional and/or biological DMARD treatment by 50% resulted in a 39% flare rate; reducing the dose of all conventional and/or biological DMARD treatment by 50% for 6 months before entirely stopping DMARD resulted in a 52% flare rate.

In summary, it is possible to taper csDMARDs, but relapse rates are relatively high with cessation. Fortunately, it is reasonably easy to regain control with reintroduction of drug.

Biologic DMARD tapering/withdrawal studies

In methotrexate-naïve RA patients or those with an inadequate response to methotrexate, biologic DMARD tapering followed by stopping is possible in a proportion of patients with early disease but more difficult in longstanding RA (see Fig. 2).

As regards longstanding TNF inhibitor therapy, dose tapering followed by stopping is possible in some patients; some patients flare upon tapering/withdrawal. A large proportion regain control after restarting the biologic; radiographic progression is higher in those who taper, although the change in radiographic score remains low. Thus, stopping longstanding TNF inhibitor therapy results in more harm, but the level of harm is relatively low and may not be clinically important. This can be an option in methotrexate-naïve RA patients in remission or on half-dose abatacept. In patients not responding on full-dose rituximab, half-dose may be an option.

bDMARD withdrawal in early, methotrexate-naïve RA

In OPTIMA, methotrexate-naïve patients with early RA received adalimumab plus methotrexate or placebo plus methotrexate for 26 weeks; 44% reached stable LDA and either continued or stopped adalimumab.¹⁸ The primary endpoint (a composite measure of DAS28 of < 3.2 at week 78 and radiographic non-progression from baseline to week 78) was met by fewer patients on methotrexate monotherapy versus patients continuing adalimumab (54% vs 70%; $p=0.0225$). Similarly, in recent-onset RA methotrexate-naïve patients, induction therapy with adalimumab plus methotrexate versus methotrexate alone, stopping the biologic was associated with more harm and less remission.¹⁹ Moreover, withdrawal of etanercept in methotrexate-naïve patients resulted in worse

outcomes (more flares and radiographic damage) compared with patients continuing on etanercept.²⁰

In established RA disease, withdrawal of biologic therapy increases the risk of disease flare in most patients.²¹⁻²⁶ In contrast, relapse is not so common after stopping biologics in recent-onset RA.

In established RA, reducing the dosing interval (tapering) of biologics is associated with better outcomes versus biologic withdrawal.²² A disease activity-guided strategy of dose reduction of adalimumab or etanercept in patients with RA and LDA resulted in more short-lived flares and minimal radiographic progression compared with usual care (no dose reduction).²⁷

In summary, tapering of biologic DMARDs is feasible. More patients flare in the taper arm and tapering has been associated with more radiographic damage. Nevertheless, the between-group difference is not great and patients can be monitored.

Predicting the development of RA and predictive models

How to predict outcomes of therapy withdrawal? AbbVie is sponsoring an ongoing phase IV trial (PREDICTRA) investigating the impact of residual inflammation detected via imaging techniques, drug levels and patient characteristics on the outcome of dose tapering of adalimumab in clinical remission RA.²⁸ The major outcome is remission and also MR and US evidence of damage over time. The trial will seek to determine if baseline characteristics of the patients make a difference to predicting RA disease.

In another study, presence of RF positivity and anti-CCP positivity predicted RA disease. Thus, reducing or stopping DMARD therapy in patients with RF- or anti-CCP-positive disease increases the risk of RA.

One study has shown that US evidence of Doppler flow in remission predicted flares in patients who withdrew their TNF inhibitor; the Doppler evidence was combined with histological data in this study.

A statistical model comprising a multi-biomarker disease activity score (a novel index based on 12 serum proteins) improved the prediction of relapses in patients with RA in stable remission undergoing DMARD tapering. Combining this model with imaging data may be useful.

In summary, withdrawing medication in RA is something to consider. However, it is vital to consider the impact upon the patient, and the long-term outcomes plus possible predictors of relapse.

Study	Population	Duration (weeks)	Remission/LDA		Taper/withdrawal	Key results	References
			Clinical	X-ray			
AVERT ABT, MTX, or ABT + MTX	MTX-naïve	78	DAS28(CRP) < 2.6 (at 12 months)		Withdrawal all RA therapy	Pts still in remission at 6 months post withdrawal: ABA + MTX: 24.7%; ABA: 28.0%; MTX: 17.0%	Emery P, et al. Ann Rheum Dis 2015;74:19-26
OPTIMA ADA, MTX, or ADA + MTX	MTX-naïve	78	DAS28 < 3.2 (at wk 22 and 26)		Withdrawal ADA	LDA and Remission maintained in ADA continuation group vs ADA withdrawal: 91% vs 81% ($p=0.036$) and 86% vs 66%; $p=0.0014$ (respectively)	Smolen JS, et al. Lancet 2014;383:321-32
ACT-RAY TCZ add-on to MTX	MTX-IR	104	DAS28(ESR) < 2.6	mTSS	Withdrawal / T2T goals TCZ	Pts still in remission at 1 year post withdrawal: TCZ+MTX: 8.6%; TCZ+PBO: 3.1% ($p=0.010$) 84.0% flared, but responded to TCZ re-initiation. Radiographic progression minimal with temporary TCZ withdrawal	Huizinga T, et al. Ann Rheum Dis 2015;74:35-43
ENCOURAGE ETN + MTX	MTX-IR	104	DAS28 < 2.6 (at 6 and 12 months)		Withdrawal ETN	Remission maintained at 24 months in 87.5% of pts who continued ETN vs 53.6% who discontinued ETN at 12 months	Yamanaka H, et al. Mod Rheumatol 2015;23:1-11

bDMARD (+csDMARD) withdrawal:

- Possible in a proportion of pts particularly in early disease
- More difficult in longstanding RA

LDA = low disease activity; ABT = abatacept; MTX = methotrexate; Pts = patients; TCZ = tocilizumab; MTX-IR = patients with an inadequate response to methotrexate; mTSS = modified total Sharp score; PBO = placebo; ETN = etanercept.

^aAdditional DMARDs, ≥ 2 courses high-dose steroid, return to open-label abatacept 10 mg/kg, or DAS28(CRP) ≥ 3.2 at 2 consecutive visits.

Figure 2. Clinical evidence for withdrawal of biologic DMARDs in RA (MTX-naïve or MTX-IR patients).



Workshop: Beyond DAS28 remission for Kiwi RA patients

Facilitator: Aviette Musin (AbbVie)

This workshop examined whether alternative targets for T2T remission exist beyond DAS28 score and explored the possibility of novel strategies for improved outcomes in Kiwi RA patients.

Team Doug White:

This group evaluated strategies and current practice around withdrawal of DMARDs in the target of drug-free remission.

- The group identified the importance of patient preference and establishing this early on in any discussions around the potential for drug-free remission. Patients may or may not be willing to have this as a goal. The PORTAL platform could discuss this concept in more depth.
- Most of the group members lack access to Power Doppler in their clinics, so rely on radiography services to provide information on disease activity based on US examinations. Unfortunately, the radiographic information often does not contain Doppler measurements. Australia has developed a series of resources designed to educate radiologists and radiographers on the US data required by rheumatologists. Longer-term, rheumatology access to Doppler US would be ideal.
- The group emphasised the importance of comprehensively assessing disease activity with disease markers before contemplating tapering. Ideally, in the longer-term, this could be incorporated into a multi-marker composite index that asks patients to quantify their risk.
- A real-world audit of clinical practice would be useful. The concept of DMARD withdrawal could be discussed with PHARMAC.
- Information for patients is an important aspect, when entering into decisions around drug withdrawal.

Team Rebecca Grainger:

This group considered whether RA patients would prefer to use other targets for remission besides DAS28 score.

- The group reflected on the PORTAL data and considered disease activity measurements. Foremost was function and participation, at an individually meaningful level.
- The group discussed patients' life priorities – immediate, medium, or longer-term.
- Employment status was discussed: how RA disease interferes with work and promotional prospects, or even employability.
- The group discussed the features of RA disease including pain, fatigue, anxiety, mood, and the concept of additional undesirable side effects associated with RA treatment. Some of these aspects have validated measurements that can

be used. There was discussion around the operationalisation of function and its measurement, as well as the concept of SMART (i.e. specific, measurable, achievable, realistic in time) goals.

- The group considered how to embed this process within a consultation: abrogation of inflammation could be used as a springboard to other goals. Use forms to collect patient information? Emailing the form to the patient for completion prior to the consultation might be helpful.
- Patient scoring and ranking of disease-related items could potentially help clinicians better understand patients' goals. The information could be used to generate self-management and Action Plans for patients to follow.
- More time in patient clinical consultations is needed to meet patient-focused targets.
- Encourage patient participation.
- Longer-term, the concept of the right education, at the right time and right level is all-important for individual patients. Health literacy is important not only for RA patients, but also for the community at large, so that people have a better understanding of the RA disease process. This would help with moving towards a more participatory paradigm, where patient-focused targets are being identified and patients are given tools to work towards the targets.

Team Mike Corkill:

This group discussed RA mortality and morbidity.

- The group identified the importance of cultivating a healthy mentality/good mental outlook for longevity and health.
- Amongst factors that have a high impact upon mortality and morbidity, and can be done within a short period of time, smoking cessation was identified as the most important, followed to a lesser degree by vaccination and infection prevention measures.
- Motivational Interviewing would be helpful when speaking to patients about smoking cessation and vaccination/infection prevention measures.
- A multitude of high-impact actions were identified that are important in the long-term and are independent of RA disease activity (e.g. weight reduction, mental wellbeing, cardiovascular risk, bone health).
- Better mental health would be the most important long-term goal for patients: Step 1, offer hope; Step 2, supply information on availability/accessibility of non-drug counselling services (e.g. Pain services, Employee Assistance Programme, Arthritis Foundation website, etc.); Step 4, monitoring.

Concluding Remarks – Andrew Harrison

In closing the plenary part of the T2T Meeting, Andrew Harrison thanked everyone for their participation; rheumatologists and trainees, rheumatology nurses, and especially the RA patients for their extremely useful contributions. He also thanked Arthritis New Zealand for providing access to RA patients, and the AbbVie team for sponsorship and facilitation of this meeting.

NURSES' BREAKOUT SESSION: TREAT TO TARGET: ENHANCING THE ROLE OF THE RHEUMATOLOGY NURSE

Workshop: Enhancing the nurse's role in assessment of patients

– Dr Michael Corkill

This session talked about those RA cases where DAS28 scores correlate with moderate disease activity, but where the component parts are inconsistent. It also considered patients with controlled RA disease who complain about one sore joint; how is this joint assessed and how does it fit into the disease context? Ideas were discussed on how best to deal with those people with controlled RA who seek advice from the rheumatology nurse about an unrelated symptom (e.g. cough, headache, itchy toes, depression).

Case histories with DAS28 scores indicating MDA, with discordant disease signals

How to treat an RA patient with 20 tender joints, no swollen joints, elevated CRP, DAS28 >4? Pain relief? It is important not to leap to a diagnostic conclusion on the basis of the symptoms; wide-ranging questions are necessary to confirm whether the disease signals fit the context.

How to treat an RA patient with one tender joint and lots of swollen joints, lasting

2 years? Administer prednisone to settle the swelling. Ask about changes over time, family history, duration of RA. Obtain X-ray data to determine if the swelling is indolent or destructive synovitis (showing progressive joint damage). US or MR evidence might be available.

How to treat an RA patient with one tender joint, no swollen joints, CRP 72. Assess for infection. CRP with weight loss may mean symptoms of cancer. Ask the patient to visit the GP.

In summary, DAS28 scores are not the only item to be aware of. The disease context and trajectory over time are important factors.

One sore joint

Determine history – is this sore joint a chronic or acute problem? Mike Corkill examines the structure proximal to the area the patient is complaining about, to define the region of pain. Does the pain worsen when the joint is manipulated?

How to deal with the RA patient presenting with an unrelated symptom?

Guard against having a preconceived concept of what this symptom could involve. Consider all pertinent information, to make an accurate diagnosis.



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