Introduction
Obesity (BMI > 30kg/m²) is increasing in incidence and is a risk factor for venous thromboembolism (VTE). There is limited and conflicting data to guide prescribing of low molecular weight heparin (LMWH) and direct oral anticoagulants (DOACs) in this patient group.

Due to the limited clinical data, and pharmacokinetic/pharmacodynamic data suggesting decreased drug exposures with obesity, ISTH suggests DOACs should not be used in patients with a weight > 120kg or BMI > 40kg/m². If DOACs are used, peak and trough drug levels should be measured.

The aims of this study were to:
1. Review available literature regarding anticoagulant dosing and efficacy in the obese and the role of drug specific levels
2. Examine anticoagulant prescribing patterns in the obese within our Local Health District
3. Assess available drug specific Xa levels in this population

Methods
We identified patients with VTE and weight > 120kg via review of attendees at the Westmead Rapid Access Clot Clinic in 2016, in addition to patients previously known to Westmead Thrombosis Clinic and Blacktown Haematology Service.

We collected demographic data, weight, height, indication, anticoagulant choice and rationale, laboratory drug monitoring, dose adjustments and clinical progress.

Results
Demographics
22 patients with weight > 120kg
Median weight 136kg (range 121-208kg)
Median BMI 45kg/m² (range 36.6-79.3) (available for 12 patients)
11/22 were female.

Choice of Anticoagulation
10/22 were commenced on a DOAC at first review: rivaroxaban (6) or apixaban (4).

Reasons a DOAC were not used; proximal lower limb DVT and concern regarding efficacy given obesity (2); malignancy (2), superior mesenteric vein thrombosis (1), cerebral sinus thrombosis (1), renal impairment (1), thrombosis on rivaroxaban (1).

2 patients on long term follow-up transitioned from warfarin to DOAC.

Enoxaparin
11/22 patients had documented therapy with enoxaparin
8/11 had at least one available Anti-Xa level
Median dose to achieve therapeutic Anti-Xa (0.6-1.2 U/ml): 0.87mg/kg (Range 0.66-1.1mg/kg)
4/11 had dose adjustments on the basis of Anti-Xa
1/11 required dose adjustment due to bleeding complications

Rivaroxaban
Published Anti-Xa Peak and Trough Levels

<table>
<thead>
<tr>
<th>Dose</th>
<th>Population</th>
<th>Method of Drug Level Assessment</th>
<th>Peak (ng/ml) (time post dose)</th>
<th>Trough (ng/ml) (time post dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10mg BD</td>
<td>Healthy subjects</td>
<td>LC/MS</td>
<td>109.4 (15 hours)</td>
<td>3.5 (12 hours)</td>
</tr>
<tr>
<td>20mg BD</td>
<td>Healthy subjects</td>
<td>LC/MS</td>
<td>5.6 (3 hours)</td>
<td>1.1 (6 hours)</td>
</tr>
</tbody>
</table>

Published Anti-Xa Peak and Trough Levels

Adverse Events
1 patient developed a new DVT on rivaroxaban, changed to warfarin therapy
1 patient had US evidence of progressive DVT on rivaroxaban, changed to apixaban
1/11 had bleeding complications on enoxaparin therapy
1/11 had recurrent subcutaneous infections on enoxaparin therapy
2/9 had menorrhagia on DOAC therapy requiring levonorgestrel intrauterine device insertion
2/10 had gastrointestinal upset: one on rivaroxaban, one on apixaban

Conclusions
There is limited data on the use of enoxaparin and DOACs at the upper extremes of weight. The limited data available on DOAC therapeutic drug levels limits monitoring in this high risk population.

Patients receiving rivaroxaban 20mg daily appear to have lower peak rivaroxaban levels than available published ranges, however trough levels fall within published ranges. 2/10 patients receiving rivaroxaban therapy had recurrent or progressive DVT.

Due to the lack of published peak ranges for apixaban, it was difficult to interpret these levels. 2/7 patients on 5mg BD dose peak levels < 100ng/ml, however trough levels for both the 2.5mg BD and 5mg BD doses fell within published ranges.

The clinical significance of these results are not clear and requires further evaluation.

Limitations and Future Directions
Audit is limited by small numbers receiving all agents, duration of follow-up and that the timing of dosing was not clearly documented in most cases.

Larger, prospective studies in the obese population are required to evaluate pharmacokinetics, pharmacodynamics and clinical outcomes in obese patients and we are commencing a multi-centre Australian and New Zealand prospective consecutive registry of obese patients requiring anticoagulation.

Conflict of Interest: Bayer paid for GM’s travel expenses and conference registration