Guidelines for low Immunoglobulin levels in adults

This Guideline is for the investigation and management of low Immunoglobulin management. Please refer to the "Paraproteins (LMGPR0013)" guidelines available via the Sheffield GP portal for the assessment of monoclonal proteins.

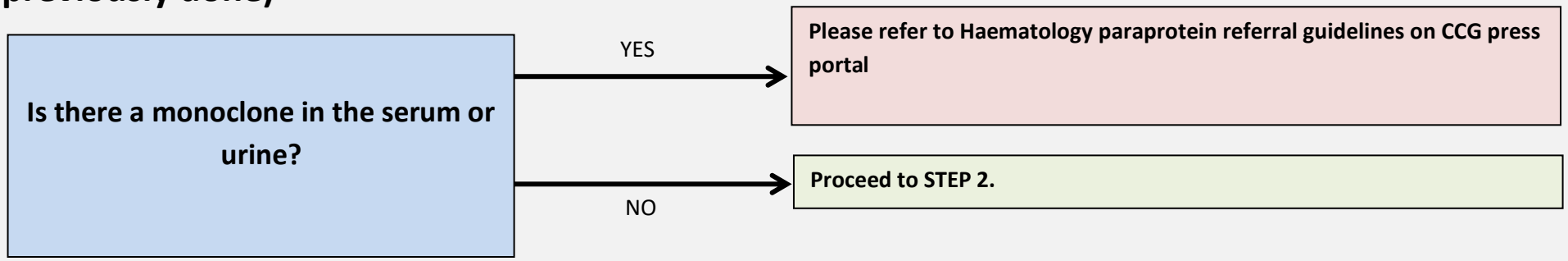
What are Immunoglobulins?

Immunoglobulins are proteins made by B cells and Plasma cells that help protect against infection.
The standard immunoglobulin profile consists of Immunoglobulins IgG, A and M.
In Sheffield Immunology laboratory we also routinely perform serum electrophoresis on all Immunoglobulin requests. Serum electrophoresis may identify evidence of monoclonal Immunoglobulin (overproduction of a single immunoglobulin by one specific plasma call population). This is known as a monoclone or paraprotein and can be seen in conditions such as Monoclonal Gammopathy of Undetermined Significance (MGUS) or Myeloma

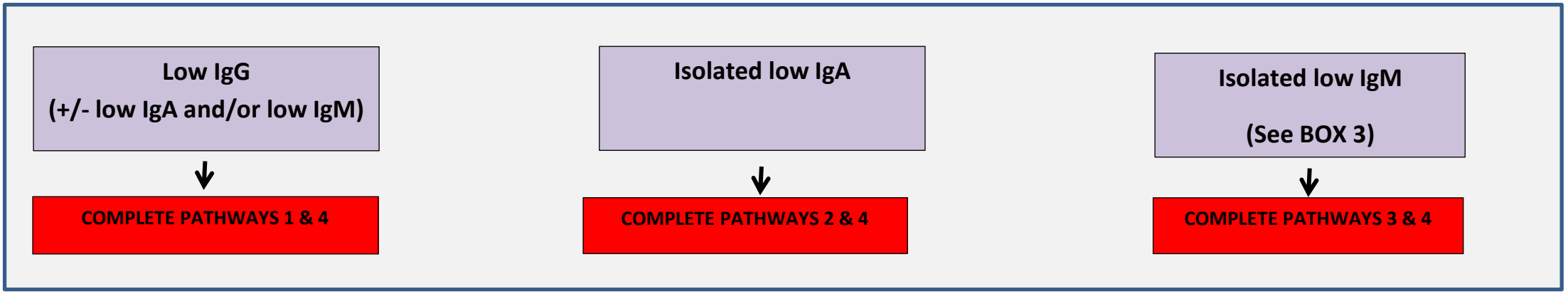
The following algorithm is a guide for managing low immunoglobulins in Primary care.
The guideline is intended for use for Adult patients only and should not be used for patients <16y old

ALGORITHM FOR ASSESSMENT AND REFERRAL OF LOW IMMUNOGLOBULINS

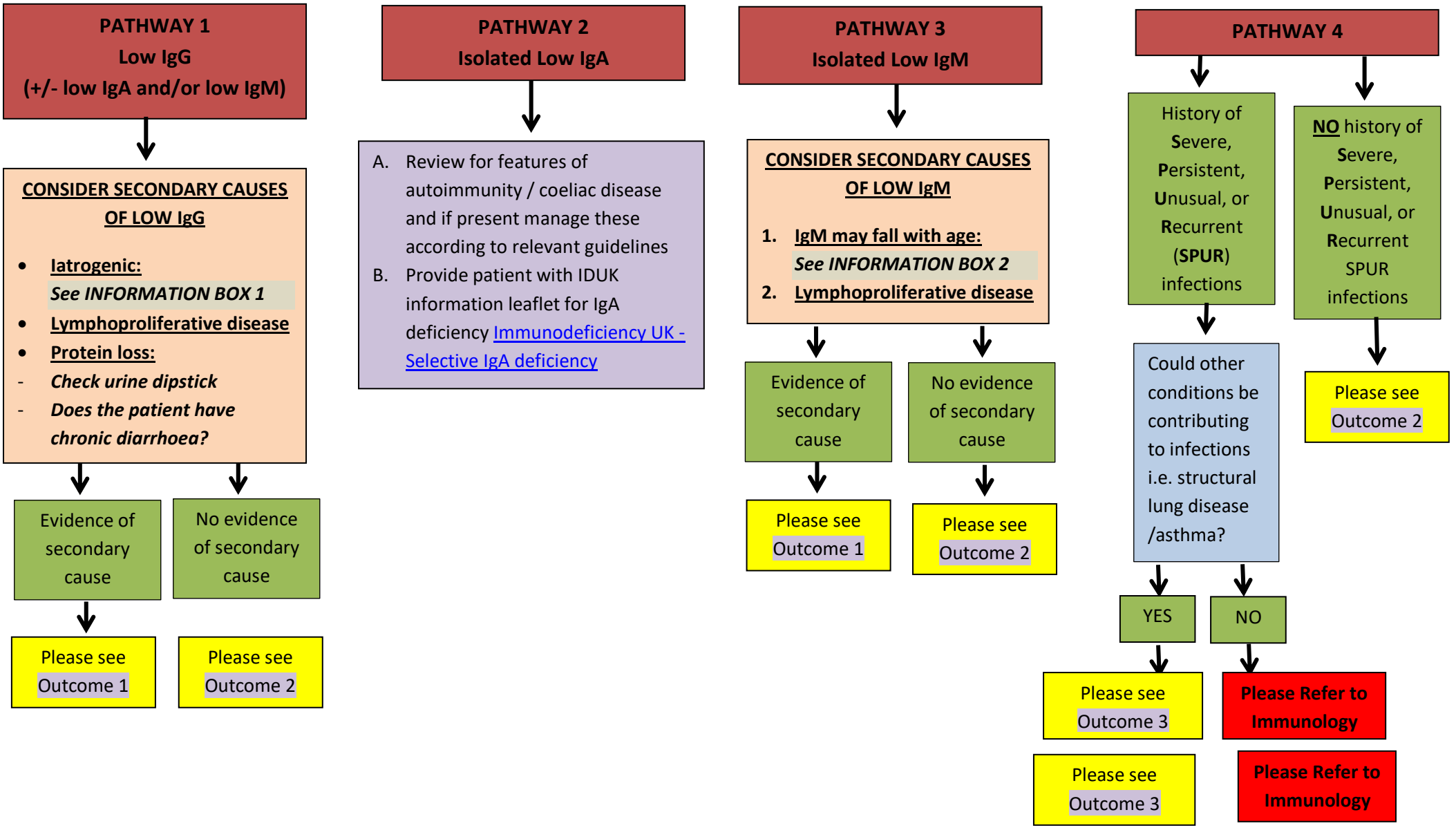
STEP 1: Request (if not already performed) and review serum/urine electrophoresis (If not previously done)



STEP 2: Which Immunoglobulin is low?



PATHWAYS 1 to 4



OUTCOMES

OUTCOME 1:

A. Consider whether secondary cause can be corrected
B. If it cannot be corrected follow OUTCOME 2
C. If B-type symptoms or lymphadenopathy/ clinically palpable splenomegaly - please liaise with Haematology

OUTCOME 2:

A. For borderline low IgG (4-6g/L) or low IgM where there is no clear secondary cause and no history of severe, persistent, unusual, or recurrent (SPUR) infection:
   - It is likely that these are incidental findings.
   - Recommend monitor serum Immunoglobulins and urine electrophoresis annually
B. If IgG <4g/L **or** SPUR infections or panhypogammaglobulinemia - refer to Immunology

OUTCOME 3:

A. Consider correcting/treating underlying cause for infections if possible
B. If infections persist or not possible to correct/treat underlying cause for infections:
   - **If IgG 4-6g/L** consider discussing with Immunology StR prior to referral.
   - **If IgG is <4g/L** please refer to Immunology clinic

Please note that urinary infections (UTIs) are not usually associated with immune deficiency. Isolated recurrent UTIs should not be referred to the

INFORMATION BOXES

BOX 1 : Drugs that can cause low IgG:

Immunosuppressive agents:	Antipsychotics:	Antiepileptics:
Abatacept Azathioprine Cyclophosphamide (and other alkylating agents) Gold D-Penicillamine Methotrexate Mycophenolate Prednisolone Rituximab (or other B-cell depleting treatment) Imatinib Sulphasalazine	Chlorpromazine Clozapine	Carbamazepine Lamotrigine Phenytoin Sodium Valproate

BOX 2: Low IgM

IgM levels can fall with advancing age even in the absence of underlying pathology.

An isolated low IgM is unlikely to be significant.

Very rarely, an isolated absent IgM can be associated with lymphoproliferative disease.*

Low IgM can also seen in uraemia and secondary to immunosuppressive drug therapy

Sources of further information:

1. IDUK Website: Information on immune deficiencieshttp://www.immunodeficiencyuk.org/
2. Sheffield Protein Reference unit website: https://www.immqas.org.uk/TestItem.asp?id=487 – Information regarding sample requirements, reference ranges and